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(54) Title: PROGNOSTIC CLASSIFICATION OF ENDOMETRIAL CANCER

(57) Abstract: The invention provided sets of genes that are expressed differentially in normal and malignant endometrium. These sets of genes can be used to discriminate between normal and malignant endometrial tissues. Accordingly, diagnosticd assays for classification of tumors, prediction of tumor outcome, selecting and monitoring treatment regimens and monitoring tumor progression/regression also are provided.

PROGNOSTIC CLASSIFICATION OF ENDOMETRIAL CANCER

Field of the Invention

The invention relates to nucleic acid microarray markers for cancer, particularly for endometrial cancer. The invention also relates to methods for diagnosing cancer as well as optimizing cancer treatment strategies.

Background of the Invention

Endometrioid endometrial adenocarcinomas are the most common gynecologic malignancy, the risk of which is increased by an abnormal endocrine environment or premalignant lesions with loss of tumor suppressor function. The 6000 deaths yearly make uterine cancer the seventh leading cause of death from malignancy in females. It is primarily a disease of postmenopausal women, although 25 percent of cases occur in women below age 50 and 5 percent below age 40 (Harrison's Principles of Internal Medicine 1998).

Although much progress has been made toward understanding the biological basis of cancer and in its diagnosis and treatment, it is still one of the leading causes of death in the United States. Inherent difficulties in the diagnosis and treatment of cancer include among other things, the existence of many different subgroups of cancer and the concomitant variation in appropriate treatment strategies to maximize the likelihood of positive patient outcome.

The prognosis of endometrial cancer depends upon stage, histologic grade, and extent of myometrial invasion. The staging of endometrial cancer requires surgery to establish the extent of disease and the depth of myometrial invasion. Peritoneal fluid should be sampled; the abdomen and pelvis explored; and pelvic and para-aortic lymphadenectomy performed depending upon the histology, grade, and depth of invasion in the uterine specimen on frozen section.

Initial evaluation of patients suspected of endometrial cancer includes a history and physical and pelvic examination followed by an endometrial biopsy or a fractional dilation and curettage. Outpatient procedures such as endometrial biopsy or aspiration curettage can be used but are definitive only when positive. Once a diagnosis is made, the options for treating endometrial cancer are assessed with respect to the needs of the patient. These options traditionally include surgical intervention, radiotherapy, chemotherapy, and adjuvant systemic therapies. Adjuvants may include but are not limited to chemotherapy, radiotherapy, and

endocrine therapies with progestational agents such as hydroxyprogesterone, megastrol, and deoxyprogesterone, and the antiestrogen tamoxifen.

It is difficult to predict from standard clinical and pathologic features the clinical course of endometrial cancer. However, it is very important in the treatment of endometrial cancer to select and implement an appropriate combination of therapeutic approaches. The available methods for designing strategies for treating endometrial cancer patients are complex and time consuming. The wide range of cancer subgroups and variations in disease progression limit the predictive ability of the healthcare professional. In addition, continuing development of novel treatment strategies and therapeutics will result in the addition of more variables to the already complex decision-making process involving matching the cancer patient with a treatment regimen that is appropriate and optimized for the cancer stage, extent of myometrial invasion, tumor growth rate, and other factors central to the individual patient's prognosis. Because of the critical importance of selecting appropriate treatment regimens for endometrial cancer patients, the development of guidelines for treatment selection is of key interest to those in the medical community and their patients. Thus, there presently is a need for objective, reproducible, and sensitive methods for predicting endometrial cancer patient outcome and selecting optimal treatment regimens.

Summary of the Invention

It now has been discovered that particular sets of genes are expressed differentially in normal and malignant endometrium. These sets of genes can be used to discriminate between normal and malignant endometrial tissues. Accordingly, diagnostic assays for classification of tumors, prediction of tumor outcome, selecting and monitoring treatment regimens, and monitoring tumor progression/regression can now be based on the expression of sets of genes.

According to one aspect of the invention, methods for diagnosing endometrial cancer in a subject suspected of having endometrial cancer are provided. The methods include obtaining from the subject an endometrial tissue sample and determining the expression of a set of nucleic acid molecules or expression products thereof in the endometrial tissue sample. The set of nucleic acid molecules includes at least two nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50. In preferred embodiments, the endometrial tissue sample is suspected of being cancerous.

In some embodiments the set of nucleic acid molecules includes more than 2, and up to all of the nucleic acid molecules set forth as SEQ ID NOs:1-50, and any number of nucleic acid sequences between these two numbers. For example, in certain embodiments the set includes at least 3, 4, 5, 10, 15, 20, 30, 40 or more nucleic acid molecules of the nucleic acid molecules set forth as SEQ ID NOs:1-50.

In other embodiments, the method further includes determining the expression of the set of nucleic acid molecules or expression products thereof in a non-cancerous endometrial tissue sample, and comparing the expression of the set of nucleic acid molecules or expression products thereof in the endometrial tissue sample suspected of being cancerous and the non-cancerous endometrial tissue sample.

The invention in another aspect provides solid-phase nucleic acid molecule arrays. The arrays have a cancer gene marker set that consists essentially of at least two and as many as all of the nucleic acid molecules set forth as SEQ ID NOs:1-50 fixed to a solid substrate. The set of nucleic acid markers can include any number of nucleic acid sequences between these two numbers, selected from SEQ ID NOs:1-50. For example, in certain embodiments the set includes at least 3, 4, 5, 10, 15, 20, 30, 40 or more nucleic acid molecules of the nucleic acid molecules set forth as SEQ ID NOs:1-50. In some embodiments, the solid-phase nucleic acid molecule array also includes at least one control nucleic acid molecule.

In certain embodiments, the solid substrate includes a material selected from the group consisting of glass, silica, aluminosilicates, borosilicates, metal oxides such as alumina and nickel oxide, various clays, nitrocellulose, or nylon. Preferably the substrate is glass.

In other embodiments, the nucleic acid molecules are fixed to the solid substrate by covalent bonding.

According to yet another aspect of the invention, protein microarrays are provided. The protein microarrays include antibodies or antigen-binding fragments thereof, that specifically bind at least two different polypeptides selected from the group consisting of SEQ ID NOs:51-100, fixed to a solid substrate. In some embodiments, the microarray comprises antibodies or antigen-binding fragments thereof, that bind specifically to least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or 50 different polypeptides selected from the group consisting of SEQ ID NOs:51-100. In certain embodiments, the microarray also includes an antibody or antigen-binding fragment thereof, that binds specifically to a cancer-associated

polypeptide other than those selected from the group consisting of SEQ ID NOs:51-100, preferably An endometrial cancer associated polypeptide. In some embodiments, the protein microarray also includes at least one control polypeptide molecule. In further embodiments, the antibodies are monoclonal or polyclonal antibodies. In other embodiments, the antibodies are chimeric, human, or humanized antibodies. In some embodiments, the antibodies are single chain antibodies. In still other embodiments, the antigen-binding fragments are $F(ab')_2$, Fab, Fd, or Fv fragments.

According to yet another aspect of the invention, protein microarrays are provided. The protein microarrays include antibodies or antigen-binding fragments thereof, that specifically bind at least two different polypeptides selected from the group consisting of SEQ ID NOs:51-100, fixed to a solid substrate. In some embodiments, the microarray comprises antibodies or antigen-binding fragments thereof, that bind specifically to least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49 or 50 different polypeptides selected from the group consisting of SEQ ID NOs:51-100. In certain embodiments, the microarray also includes an antibody or antigen-binding fragment thereof, that binds specifically to a cancer-associated polypeptide other than those selected from the group consisting of SEQ ID NOs:51-100, preferably an endometrial cancer associated polypeptide. In some embodiments, the protein microarray also includes at least one control polypeptide molecule. In further embodiments, the antibodies are monoclonal or polyclonal antibodies. In other embodiments, the antibodies are chimeric, human, or humanized antibodies. In some embodiments, the antibodies are single chain antibodies. In still other embodiments, the antigen-binding fragments are $F(ab')_2$, Fab, Fd, or Fv fragments.

In a further aspect of the invention, methods for identifying lead compounds for a pharmacological agent useful in the treatment of endometrial cancer are provided. The methods include contacting an endometrial cancer cell or tissue with a candidate pharmacological agent, and determining the expression of a set of nucleic acid molecules in the endometrial cancer cell or tissue sample under conditions which, in the absence of the candidate pharmacological agent, permit a first amount of expression of the set of nucleic acid molecules. The set of nucleic acid molecules includes at least two and as many as all of the nucleic acid molecules set forth as SEQ ID NOs:1-50. The methods also include detecting a test amount of the expression of the set of nucleic acid molecules, wherein a decrease in the test amount of expression in the presence of

the candidate pharmacological agent relative to the first amount of expression indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent that is useful in the treatment of endometrial cancer.

In some embodiments of any of the foregoing methods and products, the differences in the expression of the nucleic acid molecules are determined by nucleic acid hybridization or nucleic acid amplification methods. Preferably the nucleic acid hybridization is performed using a solid-phase nucleic acid molecule array. In other embodiments, the differences in the expression of the nucleic acid molecules are determined by protein expression analysis, preferably SELDI mass spectroscopy.

These and other aspects of the invention will be described in greater detail below.

Detailed Description of the Invention

The invention described herein relates to the identification of a set of genes expressed in endometrial cancer tissue that are predictive of the clinical outcome of the cancer. Changes in cell phenotype in cancer are often the result of one or more changes in the genome expression of the cell. Some genes are expressed in tumor cells, and not in normal cells. In addition, different genes are expressed in different subgroups of endometrial cancers, which have different prognoses and require different treatment regimens to optimize patient outcome. The differential expression of endometrial cancer genes can be examined by the assessment of nucleic acid or protein expression in the endometrial cancer tissue.

The genes identified permit, *inter alia*, rapid screening of cancer samples by nucleic acid microarray hybridization or protein expression technology to determine the expression of the specific genes and thereby to predict the outcome of the cancer. Such screening is beneficial, for example, in selecting the course of treatment to provide to the cancer patient, and to monitor the efficacy of a treatment.

The invention differs from traditional endometrial cancer diagnostic and classification techniques with respect to the speed, simplicity, and reproducibility of the cancer diagnostic assay. The invention also presents targets for drug development because it identifies genes that are differentially expressed in outcome endometrial tumors, which can be utilized in the development of drugs to treat such tumors, e.g., by reducing expression of the genes or reducing activity of proteins encoded by the genes.

The invention simplifies prognosis determination by providing an identified set of genes whose expression in endometrial cancers predicts clinical outcome as defined by tumor metastasis, recurrence, or death. In the invention RNA expression phenotyping was performed using high density microarrays generated from quantitative expression data on over 5000 (estimated 5800) genes, which have been analyzed to identify 50 specific probe sets (genes). The expression gene set has multifold uses including, but not limited to, the following examples. The expression gene set may be used as a prognostic tool for endometrial cancer patients, to make possible more finely tuned diagnosis of endometrial cancer and allow healthcare professionals to tailor treatment to individual patients' needs. The invention can also assess the efficacy of endometrial cancer treatment by determining progression or regression of endometrial cancer in patients before, during, and after endometrial cancer treatment. Another utility of the expression gene set is in the biotechnology and pharmaceutical industries' research on disease pathway discovery for therapeutic targeting. The invention can identify alterations in gene expression in endometrial cancer and can also be used to uncover and test candidate pharmaceutical agents to treat endometrial cancer.

As used herein, a subject is a human, non-human primate, cow, horse, pig, sheep, goat, dog, cat, or rodent. In all embodiments human subjects are preferred. Preferably the subject is a human either suspected of having endometrial cancer, or having been diagnosed with endometrial cancer. In a preferred embodiment of the invention the cancer is endometroid endometrial adenocarcinoma. Methods for identifying subjects suspected of having endometrial cancer may include physical examination, subject's family medical history, subject's medical history, endometrial biopsy, or a number of imaging technologies such as ultrasonography, computed tomography, magnetic resonance imaging, magnetic resonance spectroscopy, or positron emission tomography. Diagnostic methods for endometrial cancer and the clinical delineation of endometrial cancer diagnoses are well known to those of skill in the medical arts.

As used herein, endometrial tissue sample is tissue obtained from an endometrial tissue biopsy using methods well known to those of ordinary skill in the related medical arts. The phrase "suspected of being cancerous" as used herein means an endometrial cancer tissue sample believed by one of ordinary skill in the medical arts to contain cancerous cells. Methods for obtaining the sample from the biopsy include gross apportioning of a mass, microdissection, laser-based microdissection, cytologic sampling of the endometrium using a brush, aspiration curettage, fractional dilation and curettage, or other art-known cell-separation methods.

Because of the variability of the cell types in diseased-tissue biopsy material, and the variability in sensitivity of the diagnostic methods used, the sample size required for analysis may range from 1, 10, 50, 100, 200, 300, 500, 1000, 5000, 10,000, to 50,000 or more cells. The appropriate sample size may be determined based on the cellular composition and condition of the biopsy and the standard preparative steps for this determination and subsequent isolation of the nucleic acid for use in the invention are well known to one of ordinary skill in the art. An example of this, although not intended to be limiting, is that in some instances a sample from the biopsy may be sufficient for assessment of RNA expression without amplification, but in other instances the lack of suitable cells in a small biopsy region may require use of RNA conversion and/or amplification methods or other methods to enhance resolution of the nucleic acid molecules. Such methods, which allow use of limited biopsy materials, are well known to those of ordinary skill in the art and include, but are not limited to: direct RNA amplification, reverse transcription of RNA to cDNA, amplification of cDNA, or the generation of radio-labeled nucleic acids.

As used herein, the phrase "determining the expression of a set of nucleic acid molecules in the endometrial tissue" means identifying RNA transcripts in the tissue sample by analysis of nucleic acid or protein expression in the tissue sample. As used herein, "set" refers to a group of nucleic acid molecules that include 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50 different nucleic acid sequences from the group of nucleic acid sequences numbered 1 through 50 in Table 1 (SEQ ID NOs: 1-50).

The expression of the set of nucleic acid molecules in the sample from the endometrial cancer patient can be compared to the expression of the set of nucleic acid molecules in a sample of endometrial tissue that is non-cancerous. As used herein, non-cancerous endometrial tissue means tissue determined by one of ordinary skill in the medical art to have no evidence of endometrial cancer based on standard diagnostic methods including, but not limited to, histologic staining and microscopic analysis.

Nucleic acid markers for cancer are nucleic acid molecules that by their presence or absence indicate the presence of absence of endometrial cancer. In tissue, certain nucleic acid molecules are expressed at different levels depending on whether tissue is non-cancerous or cancerous.

Hybridization methods for nucleic acids are well known to those of ordinary skill in the art (see, e.g. *Molecular Cloning: A Laboratory Manual*, J. Sambrook, et al., eds., Second Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, 1989, or *Current Protocols in Molecular Biology*, F.M. Ausubel, et al., eds., John Wiley & Sons, Inc., New York). The nucleic acid molecules from an endometrial cancer tissue sample hybridize under stringent conditions to nucleic acid markers expressed in endometrial cancer. In one embodiment the markers are sets of two or more of the nucleic acid molecules as set forth in SEQ ID NOs: 1 through 50.

The endometrial cancer nucleic acid markers disclosed herein are known genes and fragments thereof. It may be desirable to identify variants of those genes, such as allelic variants or single nucleotide polymorphisms (SNPs) in tissues. Accordingly, methods for identifying endometrial cancer nucleic acid markers, including variants of the disclosed full-length cDNAs, genomic DNAs, and SNPs are also included in the invention. The methods include contacting a nucleic acid sample (such as a cDNA library, genomic library, genomic DNA isolate, etc.) with a nucleic acid probe or primer derived from one of SEQ ID NOs:1-50. The nucleic acid sample and the probe or primer hybridize to complementary nucleotide sequences of nucleic acids in the sample, if any are present, allowing detection of nucleic acids related to SEQ ID NOs: 1-50. Preferably the probe or primer is detectably labeled. The specific conditions, reagents, and the like can be selected by one of ordinary skill in the art to selectively identify nucleic acids related to sets of two or more of SEQ ID NOs:1 through 50. The isolated nucleic acid molecule can be sequenced according to standard procedures.

In addition to native nucleic acid markers (SEQ ID NOs:1-50), the invention also includes degenerate nucleic acids that include alternative codons to those present in the native materials. For example, serine residues are encoded by the codons TCA, AGT, TCC, TCG, TCT, and AGC. Each of the six codons is equivalent for the purposes of encoding a serine residue. Similarly, nucleotide sequence triplets that encode other amino acid residues include, but are not limited to: CCA, CCC, CCG, and CCT (proline codons); CGA, CGC, CGG, CGT, AGA, and AGG (arginine codons); ACA, ACC, ACG, and ACT (threonine codons); AAC and AAT (asparagine codons); and ATA, ATC, and ATT (isoleucine codons). Other amino acid residues may be encoded similarly by multiple nucleotide sequences. Thus, the invention embraces degenerate nucleic acids that differ from the biologically isolated nucleic acids in codon sequence due to the degeneracy of the genetic code.

The invention also provides modified nucleic acid molecules, which include additions, substitutions, and deletions of one or more nucleotides such as the allelic variants and SNPs described above. In preferred embodiments, these modified nucleic acid molecules and/or the polypeptides they encode retain at least one activity or function of the unmodified nucleic acid molecule and/or the polypeptides, such as hybridization, antibody binding, etc. In certain embodiments, the modified nucleic acid molecules encode modified polypeptides, preferably polypeptides having conservative amino acid substitutions. As used herein, a "conservative amino acid substitution" refers to an amino acid substitution which does not alter the relative charge or size characteristics of the protein in which the amino acid substitution is made. Conservative substitutions of amino acids include substitutions made amongst amino acids within the following groups: (a) M, I, L, V; (b) F, Y, W; (c) K, R, H; (d) A, G; (e) S, T; (f) Q, N; and (g) E, D. The modified nucleic acid molecules are structurally related to the unmodified nucleic acid molecules and in preferred embodiments are sufficiently structurally related to the unmodified nucleic acid molecules so that the modified and unmodified nucleic acid molecules hybridize under stringent conditions known to one of skill in the art.

For example, modified nucleic acid molecules that encode polypeptides having single amino acid changes can be prepared for use in the methods and products disclosed herein. Each of these nucleic acid molecules can have one, two, or three nucleotide substitutions exclusive of nucleotide changes corresponding to the degeneracy of the genetic code as described herein. Likewise, modified nucleic acid molecules that encode polypeptides having two amino acid changes can be prepared, which have, e.g., 2-6 nucleotide changes. Numerous modified nucleic acid molecules like these will be readily envisioned by one of skill in the art, including for example, substitutions of nucleotides in codons encoding amino acids 2 and 3, 2 and 4, 2 and 5, 2 and 6, and so on. In the foregoing example, each combination of two amino acids is included in the set of modified nucleic acid molecules, as well as all nucleotide substitutions that code for the amino acid substitutions. Additional nucleic acid molecules that encode polypeptides having additional substitutions (i.e., 3 or more), additions or deletions [e.g., by introduction of a stop codon or a splice site(s)] also can be prepared and are embraced by the invention as readily envisioned by one of ordinary skill in the art. Any of the foregoing nucleic acids can be tested by routine experimentation for retention of structural relation to or activity similar to the nucleic acids disclosed herein.

In the invention, standard hybridization techniques of microarray technology are utilized to assess patterns of nucleic acid expression and identify nucleic acid marker expression. Microarray technology, which is also known by other names including: DNA chip technology, gene chip technology, and solid-phase nucleic acid array technology, is well known to those of ordinary skill in the art and is based on, but not limited to, obtaining an array of identified nucleic acid probes on a fixed substrate, labeling target molecules with reporter molecules (e.g., radioactive, chemiluminescent, or fluorescent tags such as fluorescein, Cye3-dUTP, or Cye5-dUTP), hybridizing target nucleic acids to the probes, and evaluating target-probe hybridization. A probe with a nucleic acid sequence that perfectly matches the target sequence will, in general, result in detection of a stronger reporter-molecule signal than will probes with less perfect matches. Many components and techniques utilized in nucleic acid microarray technology are presented in *The Chipping Forecast*, Nature Genetics, Vol.21, Jan 1999, the entire contents of which is incorporated by reference herein.

According to the present invention, microarray substrates may include but are not limited to glass, silica, aluminosilicates, borosilicates, metal oxides such as alumina and nickel oxide, various clays, nitrocellulose, or nylon. In all embodiments a glass substrate is preferred. According to the invention, probes are selected from the group of nucleic acids including, but not limited to: DNA, genomic DNA, cDNA, and oligonucleotides; and may be natural or synthetic. Oligonucleotide probes preferably are 20 to 25-mer oligonucleotides and DNA/cDNA probes preferably are 500 to 5000 bases in length, although other lengths may be used. Appropriate probe length may be determined by one of ordinary skill in the art by following art-known procedures. In one embodiment, preferred probes are sets of two or more of the nucleic acid molecules set forth as SEQ ID NO: 1 through 50 (see also Table 1). Probes may be purified to remove contaminants using standard methods known to those of ordinary skill in the art such as gel filtration or precipitation.

In one embodiment, the microarray substrate may be coated with a compound to enhance synthesis of the probe on the substrate. Such compounds include, but are not limited to, oligoethylene glycols. In another embodiment, coupling agents or groups on the substrate can be used to covalently link the first nucleotide or oligonucleotide to the substrate. These agents or groups may include, but are not limited to: amino, hydroxy, bromo, and carboxy groups. These reactive groups are preferably attached to the substrate through a hydrocarbyl radical such as an alkylene or phenylene divalent radical, one valence position occupied by the chain bonding and

the remaining attached to the reactive groups. These hydrocarbyl groups may contain up to about ten carbon atoms, preferably up to about six carbon atoms. Alkylene radicals are usually preferred containing two to four carbon atoms in the principal chain. These and additional details of the process are disclosed, for example, in U.S. Patent 4,458,066, which is incorporated by reference in its entirety.

In one embodiment, probes are synthesized directly on the substrate in a predetermined grid pattern using methods such as light-directed chemical synthesis, photochemical deprotection, or delivery of nucleotide precursors to the substrate and subsequent probe production.

In another embodiment, the substrate may be coated with a compound to enhance binding of the probe to the substrate. Such compounds include, but are not limited to: polylysine, amino silanes, amino-reactive silanes (Chipping Forecast, 1999) or chromium (Gwynne and Page, 2000). In this embodiment, presynthesized probes are applied to the substrate in a precise, predetermined volume and grid pattern, utilizing a computer-controlled robot to apply probe to the substrate in a contact-printing manner or in a non-contact manner such as ink jet or piezo-electric delivery. Probes may be covalently linked to the substrate with methods that include, but are not limited to, UV-irradiation. In another embodiment probes are linked to the substrate with heat.

Targets are nucleic acids selected from the group, including but not limited to: DNA, genomic DNA, cDNA, RNA, mRNA and may be natural or synthetic. In all embodiments, nucleic acid molecules from human endometrial tissue are preferred. The tissue may be obtained from a subject or may be grown in culture (e.g. from a endometrial cancer cell line).

In embodiments of the invention one or more control nucleic acid molecules are attached to the substrate. Preferably, control nucleic acid molecules allow determination of factors including but not limited to: nucleic acid quality and binding characteristics; reagent quality and effectiveness; hybridization success; and analysis thresholds and success. Control nucleic acids may include but are not limited to expression products of genes such as housekeeping genes or fragments thereof.

To select a set of tumor markers, the expression data generated by, for example, microarray analysis of gene expression, preferably is analyzed to determine which genes in different groups of cancer tissues are significantly differentially expressed. In the methods disclosed herein, the significance of gene expression was determined using Permax computer

software, although any standard statistical package that can discriminate significant differences in expression may be used. Permax performs permutation 2-sample t-tests on large arrays of data. For high dimensional vectors of observations, the Permax software computes t-statistics for each attribute, and assesses significance using the permutation distribution of the maximum and minimum overall attributes.

In one embodiment of the invention, expression of nucleic acid markers is used to select clinical treatment paradigms for endometrial cancer. Treatment options, as described herein, may include but are not limited to: radiotherapy, chemotherapy, adjuvant therapy, or any combination of the aforementioned methods. Aspects of treatment that may vary include, but are not limited to: dosages, timing of administration, or duration or therapy; and may or may not be combined with other treatments, which may also vary in dosage, timing, or duration. Another treatment for endometrial cancer is surgery, which can be utilized either alone or in combination with any of the aforementioned treatment methods. One of ordinary skill in the medical arts may determine an appropriate treatment paradigm based on evaluation of differential expression of sets of two or more of the nucleic acid targets ste forth as SEQ ID NOs:1-50. Cancers that express markers that are indicative of a more aggressive cancer or poor prognosis may be treated with more aggressive therapies.

Progression or regression of endometrial cancer is determined by comparison of two or more different endometrial cancer tissue samples taken at two or more different times from a subject. For example, progression or regression may be evaluated by assessments of expression of sets of two or more of the nucleic acid targets, including but not limited to SEQ ID NOs:1-50, in an endometrial cancer tissue sample from a subject before, during, and following treatment for endometrial cancer.

In another embodiment, novel pharmacological agents useful in the treatment of endometrial cancer can be identified by assessing variations in the expression of sets of two or more endometrial cancer nucleic acid markers, from among SEQ ID NOs:1-50, prior to and after contacting endometrial cancer cells or tissues with candidate pharmacological agents for the treatment of endometrial cancer. The cells may be grown in culture (e.g. from an endometrial cancer cell line), or may be obtained from a subject, (e.g. in a clinical trial of candidate pharmaceutical agents to treat endometrial cancer). Alterations in expression of two or more sets of endometrial cancer nucleic acid markers, from among SEQ ID NOs:1-50, in endometrial cancer cells or tissues tested before and after contact with a candidate pharmacological agent to

treat endometrial cancer, indicate progression, regression, or stasis of the endometrial cancer thereby indicating efficacy of candidate agents and concomitant identification of lead compounds for therapeutic use in endometrial cancer.

The invention further provides efficient methods of identifying pharmacological agents or lead compounds for agents active at the level of endometrial cancer cellular function. Generally, the screening methods involve assaying for compounds that beneficially alter endometrial cancer nucleic acid molecule expression. Such methods are adaptable to automated, high-throughput screening of compounds.

The assay mixture comprises a candidate pharmacological agent. Typically, a plurality of assay mixtures are run in parallel with different agent concentrations to obtain a different response to the various concentrations. Typically, one of these concentrations serves as a negative control, i.e., at zero concentration of agent or at a concentration of agent below the limits of assay detection. Candidate agents encompass numerous chemical classes, although typically they are organic compounds. Preferably, the candidate pharmacological agents are small organic compounds, i.e., those having a molecular weight of more than 50 yet less than about 2500, preferably less than about 1000 and, more preferably, less than about 500. Candidate agents comprise functional chemical groups necessary for structural interactions with polypeptides and/or nucleic acids, and typically include at least an amine, carbonyl, hydroxyl, or carboxyl group, preferably at least two of the functional chemical groups and more preferably at least three of the functional chemical groups. The candidate agents can comprise cyclic carbon or heterocyclic structure and/or aromatic or polyaromatic structures substituted with one or more of the above-identified functional groups. Candidate agents also can be biomolecules such as peptides, saccharides, fatty acids, sterols, isoprenoids, purines, pyrimidines, derivatives or structural analogs of the above, or combinations thereof and the like. Where the agent is a nucleic acid, the agent typically is a DNA or RNA molecule, although modified nucleic acids as defined herein are also contemplated.

Candidate agents are obtained from a wide variety of sources including libraries of synthetic or natural compounds. For example, numerous means are available for random and directed synthesis of a wide variety of organic compounds and biomolecules, including expression of randomized oligonucleotides, synthetic organic combinatorial libraries, phage display libraries of random peptides, and the like. Alternatively, libraries of natural compounds in the form of bacterial, fungal, plant, and animal extracts are available or readily produced.

Additionally, natural and synthetically produced libraries and compounds can be readily be modified through conventional chemical, physical, and biochemical means. Further, known pharmacological agents may be subjected to directed or random chemical modifications such as acylation, alkylation, esterification, amidification, etc. to produce structural analogs of the agents.

A variety of other reagents also can be included in the mixture. These include reagents such as salts, buffers, neutral proteins (e.g., albumin), detergents, etc. which may be used to facilitate optimal protein-protein and/or protein-nucleic acid binding. Such a reagent may also reduce non-specific or background interactions of the reaction components. Other reagents that improve the efficiency of the assay such as protease, inhibitors, nuclease inhibitors, antimicrobial agents, and the like may also be used.

The mixture of the foregoing assay materials is incubated under conditions whereby, the anti-endometrial cancer candidate agent specifically binds the cellular binding target, a portion thereof or analog thereof. The order of addition of components, incubation temperature, time of incubation, and other paameters of the assay may be readily determined. Such experimentation merely involves optimization of the assay parameters, not the fundamental composition of the assay. Incubation temperatures typically are between 4°C and 40°C. Incubation times preferably are minimized to facilitate rapid, high throughput screening, and typically are between 0.1 and 10 hours.

After incubation, the presence or absence of specific binding between the anti-endometrial cancer candidate agent and one or more binding targets is detected by any convenient method available to the user. For cell-free binding type assays, a separation step is often used to separate bound from unbound components. The separation step may be accomplished in a variety of ways. Conveniently, at least one of the components is immobilized on a solid substrate, from which the unbound components may be easily separated. The solid substrate can be made of a wide variety of materials and in a wide variety of shapes, e.g., microtiter plate, microbead, dipstick, resin particle, etc. The substrate preferably is chosen to maximize signal-to-noise ratios, primarily to minimize background binding, as well as for ease of separation and cost.

Separation may be effected for example, by removing a bead or dipstick from a reservoir, emptying or diluting a reservoir such as a microtiter plate well, rinsing a bead, particle, chromotograpic column or filter with a wash solution or solvent. The separation step preferably

includes multiple rinses or washes. For example, when the solid substrate is a microtiter plate, the wells may be washed several times with a washing solution, which typically includes those components of the incubation mixture that do not participate in specific bindings such as salts, buffer, detergent, non-specific protein, etc. Where the solid substrate is a magnetic bead, the beads may be washed one or more times with a washing solution and isolated using a magnet.

Detection may be effected in any convenient way for cell-based assays such as two- or three-hybrid screens. The transcript resulting from a reporter gene transcription assay of the anti-cancer agent binding to a target molecule typically encodes a directly or indirectly detectable product, e.g., β-galactosidase activity, luciferase activity, and the like. For cell-free binding assays, one of the components usually comprises, or is coupled to, a detectable label. A wide variety of labels can be used, such as those that provide direct detection (e.g., radioactivity, luminescence, optical, or electron density, etc) or indirect detection (e.g., epitope tag such as the FLAG epitope, enzyme tag such as horseseradish peroxidase, etc.). The label may be bound to an anti-cancer agent binding partner, or incorporated into the structure of the binding partner.

A variety of methods may be used to detect the label, depending on the nature of the label and other assay components. For example, the label may be detected while bound to the solid substrate or subsequent to separation from the solid substrate. Labels may be directly detected through optical or electron density, radioactive emissions, nonradiative energy transfers, etc. or indirectly detected with antibody conjugates, strepavidin-biotin conjugates, etc. Methods for detecting the labels are well known in the art.

The invention provides endometrial cancer gene-specific binding agents, methods of identifying and making such agents, and their use in diagnosis, therapy and pharmaceutical development. For example, endometrial cancer gene-specific pharmacological agents are useful in a variety of diagnostic and therapeutic applications as described herein. In general, the specificity of an endometrial cancer gene binding to a binding agent is shown by binding equilibrium constants. Targets that are capable of selectively binding an endometrial cancer gene preferably have binding equilibrium constants of at least about 10^7 M^{-1}, more preferably at least about 10^8 M^{-1}, and most preferably at least about 10^9 M^{-1}. The wide variety of cell-based and cell-free assays may be used to demonstrate endometrial cancer gene-specific binding. Cell-based assays include one, two and three hybrid screens, assays in which endometrial cancer gene-mediated transcription is inhibited or increased, etc. Cell-free assays include endometrial cancer gene-protein binding assays, immunoassays, etc. Other assays useful for screening

agents which bind endometrial cancer polypeptides include fluorescence resonance energy transfer (FRET), and electrophoretic mobility shift analysis (EMSA).

In another aspect of the invention, pre- and post-treatment alterations in expression of two or more sets of endometrial cancer nucleic acid markers including, but not limited to, SEQ ID NOs:1-50 in endometrial cancer cells or tissues may be used to assess treatment parameters including, but not limited to: dosage, method of administration, timing of administration, and combination with other treatments as described herein.

Candidate pharmacological agents may include antisense oligonucleotides that selectively bind to an endometrial cancer nucleic acid marker molecule, as identified herein, to reduce the expression of the marker molecules in endometrial cancer cells and tissues. One of ordinary skill in the art can test of the effects of a reduction of expression of endometrial cancer nucleic acid marker sequences *in vivo* or *in vitro*, to determine the efficacy of one or more antisense oligonucleotides.

As used herein, the term "antisense oligonucleotide" or "antisense" describes an oligonucleotide that is an oligoribonucleotide, oligodeoxyribonucleotide, modified oligoribonucleotide, or modified oligodeoxyribonucleotide, which hybridizes under physiological conditions to DNA comprising a particular gene or to an mRNA transcript of that gene and, thereby, inhibits the transcription of that gene and/or the translation of that mRNA. The antisense molecules are designed so as to interfere with transcription or translation of a target gene upon hybridization with the target gene or transcript. Those skilled in the art will recognize that the exact length of the antisense oligonucleotide and its degree of complementarity with its target will depend upon the specific target selected, including the sequence of the target and the particular bases which comprise that sequence. It is preferred that the antisense oligonucleotide be constructed and arranged so as to bind selectively with the target under physiological conditions, i.e., to hybridize substantially more to the target sequence than to any other sequence in the target cell under physiological conditions.

Based upon the sequences of endometrial cancer expressed nucleic acids, or upon allelic or homologous genomic and/or cDNA sequences, one of skill in the art can easily choose and synthesize any of a number of appropriate antisense molecules for use in accordance with the present invention. In order to be sufficiently selective and potent for inhibition, such antisense oligonucleotides should comprise at least 10 and, more preferably, at least 15 consecutive bases that are complementary to the target, although in certain cases modified oligonucleotides as

short as 7 bases in length have been used successfully as antisense oligonucleotides (Wagner et al., 1996). Most preferably, the antisense oligonucleotides comprise a complementary sequence of 20-30 bases. Although oligonucleotides may be chosen that are antisense to any region of the gene or mRNA transcripts, in preferred embodiments the antisense oligonucleotides correspond to N-terminal or 5' upstream sites such as translation initiation, transcription initiation, or promoter sites. In addition, 3'-untranslated regions may be targeted. Targeting to mRNA splicing sites has also been used in the art but may be less preferred if alternative mRNA splicing occurs. In addition, the antisense is targeted, preferably, to sites in which mRNA secondary structure is not expected (see, e.g., Sainio et al., 1994) and at which proteins are not expected to bind. Finally, although the listed sequences are cDNA sequences, one of ordinary skill in the art may easily derive the genomic DNA corresponding to the cDNA of an endometrial cancer expressed polypeptide. Thus, the present invention also provides for antisense oligonucleotides that are complementary to the genomic DNA corresponding to endometrial cancer expressed nucleic acids. Similarly, the use of antisense to allelic or homologous cDNAs and genomic DNAs are enabled without undue experimentation.

In one set of embodiments, the antisense oligonucleotides of the invention may be composed of "natural" deoxyribonucleotides, ribonucleotides, or any combination thereof. That is, the 5' end of one native nucleotide and the 3' end of another native nucleotide may be covalently linked, as in natural systems, via a phosphodiester internucleoside linkage. These oligonucleotides may be prepared by art-recognized methods, which may be carried out manually or by an automated synthesizer. They also may be produced recombinantly by vectors.

In preferred embodiments, however, the antisense oligonucleotides of the invention also may include "modified" oligonucleotides. That is, the oligonucleotides may be modified in a number of ways that do not prevent them from hybridizing to their target but which enhance their stability or targeting or which otherwise enhance their therapeutic effectiveness. The term "modified oligonucleotide" as used herein describes an oligonucleotide in which (1) at least two of its nucleotides are covalently linked via a synthetic internucleoside linkage (i.e., a linkage other than a phosphodiester linkage between the 5' end of one nucleotide and the 3' end of another nucleotide) and/or (2) a chemical group not normally associated with nucleic acids has been covalently attached to the oligonucleotide. Preferred synthetic internucleoside linkages are phosphorothioates, alkylphosphonates, phosphorodithioates, phosphate esters,

alkylphosphonothioates, phosphoramidates, carbamates, carbonates, phosphate triesters, acetamidates, carboxymethyl esters, and peptides.

The term "modified oligonucleotide" also encompasses oligonucleotides with a covalently modified base and/or sugar. For example, modified oligonucleotides include oligonucleotides having backbone sugars that are covalently attached to low molecular weight organic groups other than a hydroxyl group at the 3' position and other than a phosphate group at the 5' position. Thus modified oligonucleotides may include a 2'-O-alkylated ribose group. In addition, modified oligonucleotides may include sugars such as arabinose instead of ribose. The present invention, thus, contemplates pharmaceutical preparations containing modified antisense molecules that are complementary to and hybridizable with, under physiological conditions, endometrial cancer expressed nucleic acids, together with pharmaceutically acceptable carriers.

Antisense oligonucleotides may be administered as part of a pharmaceutical composition. Such a pharmaceutical composition may include the antisense oligonucleotides in combination with any standard physiologically and/or pharmaceutically acceptable carriers which are known in the art. The compositions should be sterile and contain a therapeutically effective amount of the antisense oligonucleotides in a unit of weight or volume suitable for administration to a patient. The term "pharmaceutically acceptable" means a non-toxic material that does not interfere with the effectiveness of the biological activity of the active ingredients. The term "physiologically acceptable" refers to a non-toxic material that is compatible with a biological system such as a cell, cell culture, tissue, or organism. The characteristics of the carrier will depend on the route of administration. Physiologically and pharmaceutically acceptable carriers include diluents, fillers, salts, buffers, stabilizers, solubilizers, and other materials, which are well known in the art.

Expression of endometrial cancer nucleic acid molecules can also be determined using protein measurement methods to determine expression of SEQ ID NOs:1-50, e.g., by determining the expression of polypeptides encoded by SEQ ID NOs:1-50 (SEQ ID NOs: 51-100). Preferred methods of specifically and quantitatively measuring proteins include, but are not limited to: mass spectroscopy-based methods such as surface enhanced laser desorption ionization (SELDI; e.g., Ciphergen ProteinChip System), non-mass spectroscopy-based methods, and immunohistochemistry-based methods such as 2-dimensional gel electrophoresis.

SELDI methodology may, through procedures known to those of ordinary skill in the art, be used to vaporize microscopic amounts of tumor protein and to create a "fingerprint" of

individual proteins, thereby allowing simultaneous measurement of the abundance of many proteins in a single sample. Preferably SELDI-based assays may be utilized to classify endometrial cancer tumors. Such assays preferably include, but are not limited to the following examples. Gene products discovered by RNA microarrays may be selectively measured by specific (antibody mediated) capture to the SELDI protein disc (e.g., selective SELDI). Gene products discovered by protein screening (e.g., with 2-D gels), may be resolved by "total protein SELDI" optimized to visualize those particular markers of interest from among SEQ ID NOs:1-50. Predictive models of tumor classification from SELDI measurement of multiple markers from among SEQ ID NOs:1-50 may be utilized for the SELDI strategies. In an additional embodiment a set of endometrioid endometrial adenocarcinoma tissues may be preferably utilized to determine the risk classification of endometrial cancer based on SELDI results.

The invention also involves agents such as polypeptides that bind to endometrial cancer-associated polypeptides, i.e., SEQ ID NOs:51-100. Such binding agents can be used, for example, in screening assays to detect the presence or absence of endometrial cancer-associated polypeptides and complexes of endometrial cancer-associated polypeptides and their binding partners and in purification protocols to isolate endometrial cancer-associated polypeptides and complexes of endometrial cancer-associated polypeptides and their binding partners. Such agents also may be used to inhibit the native activity of the endometrial cancer-associated polypeptides, for example, by binding to such polypeptides.

The invention, therefore, embraces peptide binding agents which, for example, can be antibodies or fragments of antibodies having the ability to selectively bind to endometrial cancer-associated polypeptides. Antibodies include polyclonal and monoclonal antibodies, prepared according to conventional methodology.

Significantly, as is well-known in the art, only a small portion of an antibody molecule, the paratope, is involved in the binding of the antibody to its epitope (see, in general, Clark, W.R. (1986) The Experimental Foundations of Modern Immunology Wiley & Sons, Inc., New York; Roitt, I. (1991) Essential Immunology, 7th Ed., Blackwell Scientific Publications, Oxford). The pFc' and Fc regions, for example, are effectors of the complement cascade but are not involved in antigen binding. An antibody from which the pFc' region has been enzymatically cleaved, or which has been produced without the pFc' region, designated an $F(ab')_2$ fragment, retains both of the antigen binding sites of an intact antibody. Similarly, an antibody from which the Fc region has been enzymatically cleaved, or which has been produced

without the Fc region, designated an Fab fragment, retains one of the antigen binding sites of an intact antibody molecule. Proceeding further, Fab fragments consist of a covalently bound antibody light chain and a portion of the antibody heavy chain denoted Fd. The Fd fragments are the major determinant of antibody specificity (a single Fd fragment may be associated with up to ten different light chains without altering antibody specificity) and Fd fragments retain epitope-binding ability in isolation.

Within the antigen-binding portion of an antibody, as is well-known in the art, there are complementarity determining regions (CDRs), which directly interact with the epitope of the antigen, and framework regions (FRs), which maintain the tertiary structure of the paratope (see, in general, Clark, 1986; Roitt, 1991). In both the heavy chain Fd fragment and the light chain of IgG immunoglobulins, there are four framework regions (FR1 through FR4) separated respectively by three complementarity determining regions (CDR1 through CDR3). The CDRs, and in particular the CDR3 regions, and more particularly the heavy chain CDR3, are largely responsible for antibody specificity.

It is now well-established in the art that the non-CDR regions of a mammalian antibody may be replaced with similar regions of conspecific or heterospecific antibodies while retaining the epitopic specificity of the original antibody. This is most clearly manifested in the development and use of "humanized" antibodies in which non-human CDRs are covalently joined to human FR and/or Fc/pFc' regions to produce a functional antibody. See, e.g., U.S. patents 4,816,567, 5,225,539, 5,585,089, 5,693,762 and 5,859,205.

Fully human monoclonal antibodies also can be prepared by immunizing mice transgenic for large portions of human immunoglobulin heavy and light chain loci. Following immunization of these mice (e.g., XenoMouse (Abgenix), HuMAb mice (Medarex/GenPharm)), monoclonal antibodies can be prepared according to standard hybridoma technology. These monoclonal antibodies will have human immunoglobulin amino acid sequences and therefore will not provoke human anti-mouse antibody (HAMA) responses when administered to humans.

Thus, as will be apparent to one of ordinary skill in the art, the present invention also provides for $F(ab')_2$, Fab, Fv and Fd fragments; chimeric antibodies in which the Fc and/or FR and/or CDR1 and/or CDR2 and/or light chain CDR3 regions have been replaced by homologous human or non-human sequences; chimeric $F(ab')_2$ fragment antibodies in which the FR and/or CDR1 and/or CDR2 and/or light chain CDR3 regions have been replaced by homologous human or non-human sequences; chimeric Fab fragment antibodies in which the FR and/or CDR1

and/or CDR2 and/or light chain CDR3 regions have been replaced by homologous human or non-human sequences; and chimeric Fd fragment antibodies in which the FR and/or CDR1 and/or CDR2 regions have been replaced by homologous human or non-human sequences. The present invention also includes so-called single chain antibodies.

Thus, the invention involves polypeptides of numerous size and type that bind specifically to polypeptides selected from SEQ ID NOs:51-100, and complexes of both endometrial cancer-associated polypeptides and their binding partners. These polypeptides may be derived also from sources other than antibody technology. For example, such polypeptide binding agents can be provided by degenerate peptide libraries which can be readily prepared in solution, in immobilized form or as phage display libraries. Combinatorial libraries also can be synthesized of peptides containing one or more amino acids. Libraries further can be synthesized of peptoids and non-peptide synthetic moieties.

Phage display can be particularly effective in identifying binding peptides useful according to the invention. Briefly, one prepares a phage library (using e.g. m13, fd, or lambda phage), displaying inserts from 4 to about 80 amino acid residues using conventional procedures. The inserts may represent, for example, a completely degenerate or biased array. One then can select phage-bearing inserts which bind to the endometrial cancer-associated polypeptide. This process can be repeated through several cycles of reselection of phage that bind to the endometrial cancer-associated polypeptide. Repeated rounds lead to enrichment of phage bearing particular sequences. DNA sequence analysis can be conducted to identify the sequences of the expressed polypeptides. The minimal linear portion of the sequence that binds to the endometrial cancer-associated polypeptide can be determined. One can repeat the procedure using a biased library containing inserts containing part or all of the minimal linear portion plus one or more additional degenerate residues upstream or downstream thereof. Yeast two-hybrid screening methods also may be used to identify polypeptides that bind to the endometrial cancer-associated polypeptides.

Thus, the endometrial cancer-associated polypeptides of the invention, including fragments thereof, can be used to screen peptide libraries, including phage display libraries, to identify and select peptide binding partners of the endometrial cancer-associated polypeptides of the invention. Such molecules can be used, as described, for screening assays, for purification protocols, for interfering directly with the functioning of endometrial cancer-associated polypeptides and for other purposes that will be apparent to those of ordinary skill in the art. For

example, isolated endometrial cancer-associated polypeptides can be attached to a substrate (e.g., chromatographic media, such as polystyrene beads, a filter, or an array substrate), and then a solution suspected of containing the binding partner may be applied to the substrate. If a binding partner that can interact with endometrial cancer-associated polypeptides is present in the solution, then it will bind to the substrate-endometrial cancer-associated polypeptide. The binding partner then may be isolated.

As detailed herein, the foregoing antibodies and other binding molecules may be used for example, to identify tissues expressing protein or to purify protein. Antibodies also may be coupled to specific diagnostic labeling agents for imaging of cells and tissues that express endometrial cancer-associated polypeptides or to therapeutically useful agents according to standard coupling procedures. Diagnostic agents include, but are not limited to, barium sulfate, iocetamic acid, iopanoic acid, ipodate calcium, diatrizoate sodium, diatrizoate meglumine, metrizamide, tyropanoate sodium and radiodiagnostics including positron emitters such as fluorine-18 and carbon-11, gamma emitters such as iodine-123, technitium-99m, iodine-131 and indium-111, nuclides for nuclear magnetic resonance such as fluorine and gadolinium.

The invention further includes protein microarrays for analyzing expression of endometrial cancer-associated peptides selected from SEQ ID NOs:51-100. In this aspect of the invention, standard techniques of microarray technology are utilized to assess expression of the endometrial cancer-associated polypeptides and/or identify biological constituents that bind such polypeptides. The constituents of biological samples include antibodies, lymphocytes (particularly T lymphocytes), and the like. Protein microarray technology, which is also known by other names including: protein chip technology and solid-phase protein array technology, is well known to those of ordinary skill in the art and is based on, but not limited to, obtaining an array of identified peptides or proteins on a fixed substrate, binding target molecules or biological constituents to the peptides, and evaluating such binding. See, e.g., G. MacBeath and S.L. Schreiber, "Printing Proteins as Microarrays for High-Throughput Function Determination," *Science* 289(5485):1760-1763, 2000.

Preferably antibodies or antigen binding fragments thereof that specifically bind polypeptides selected from the group consisting of SEQ ID NOs:51-100 are attached to the microarray substrate in accordance with standard attachment methods known in the art. These arrays can be used to quantify the expression of the polypeptides identified herein.

In some embodiments of the invention, one or more control peptide or protein molecules are attached to the substrate. Preferably, control peptide or protein molecules allow determination of factors such as peptide or protein quality and binding characteristics, reagent quality and effectiveness, hybridization success, and analysis thresholds and success.

The use of such methods to determine expression of endometrial cancer nucleic acids from among SEQ ID NOs:1-50 and/or proteins from among SEQ ID Nos:51-100 can be done with routine methods known to those of ordinary skill in the art and the expression determined by protein measurement methods may be used as a prognostic method for selecting treatment strategies for endometrial cancer patients.

Examples

To establish a prognostic tool for designing endometrial cancer treatment regimens, expression patterns in primary endometrialcancer specimens were assessed and correlated with clinical outcome.

Tissue processing:

RNA isolated from normal cycling (proliferative, n=2; secretory, n=2) and neoplastic (endometrioid adenocarcinoma, n=10) human endometrial specimens was reverse transcribed and resultant cDNA used for in *vitro* transcriptional synthesis of fluorescently labeled nucleic acid probes according to manufacturer's instructions. Each resultant tissue-derived probe was then separately hybridized to an Affymetrix HuFL human expression array and hybridization images analyzed with Affymetrix software to generate a data matrix of named probes by quantitative expression level in each tissue.

Data Normalization:

Average differences for each sample were rescaled to sum to 3,000,000 over all genes. Then the average differences with an Affymetrix call of Absent or Marginal were set to 20, and average differences with a call of Present but with less than 20 were also set to 20. This resulted in a dataset truncated on the left tail at a value of 20, in which only genes determined to be "present" by the Affymetrix call were included as positive expression values.

Permax Test:

Standard pooled variance t-statistics comparing the 4 normal samples to the 10 tumor samples were computed separately for each gene from their log values. Log values were used because it is natural to think of differences between tissue types as a multiplicative effect or ratio increase/decrease. Only genes with at least 2 values > 20 were considered (3665 genes), since the t statistic is undefined for genes with all values = 20, and the statistic is either 1.69 or -.62 with only one value not equal to 20, regardless of the value.

The permutation distribution was used to assess the significance of t-statistics calculated for each gene in the dataset (Permax test). The customized program written in S-plus language to calculate Permax is a data analysis software tool for testing the significance of gene expression. It has been presented by Mutter, et al., 8th International Workshop on Chromosomes in Solid Tumors, Tucson, AZ, 2000; and is available online[2] at biowww.dfci.harvard.edu/~gray/permax.html and from Robert J. Gray, Department of Biostatistical Science, Dana-Farber Cancer Institute, 44 Binney Street Boston, MA 02115. Permax details enclosed therein are incorporated by reference herein.. In this approach all 1001 possible ways of dividing the 14 samples into two groups of sizes 4 and 10 were considered. For each of these, the t-statistics were computed for each gene. With unequal group sizes, these distributions are not symmetric, so the significance was assessed separately in each direction. To control the overall error rate, the distributions of the maximum and minimum t-statistics over the genes were used. That is, for each gene, the p-value in the direction with expression higher (lower) in normals is the proportion of permutations with the minimum (maximum) t statistic over all genes less than (greater than) or equal to the observed value for the particular gene. A test declaring as significant any genes with say p<.50 then guarantees that the chance of any false positives being selected is <50%.

The t statistics have a tendency to preferentially select genes with very small variances within a group. Because of this it may be appropriate to also require minimum criteria for differences between the group means. After determining the most significant genes from the t statistics, those genes with absolute differences between means <100, and ratios of means <3 were identified.

Table 1 is a spreadsheet identifying 50 genes which discriminate normal cycling from malignant endometrium.

Table 1

SEQ ID NO	GeneCode	Permax GPT	Fold GPT	Delta GPT	ChrBand	NLX GPT	TX GPT	AffyProbe Set	LocusLink	GenBank	ABREV	Title (from Unigene)
1	x6235	0.042	8.9	157.3	17q21	177	20	D88213_at	314	D88213	AOC2	amine oxidase, copper containing 2 (retina-specific)
2	x4535	0.2218	11.6	344.8	19q13.1	377	32	HG162-HT3165_at	558	M76125	AXL	AXL receptor tyrosine kinase
3	x2035	0.2727	45.9	898.1	11p15.5	20	918	M91083_at	8045	M91083	C11ORF13	chromosome 11 open reading frame 13
4	x3265	0.468	10.1	1590.5	12p13	1766	175	D13639_at	894	D13639	CCND2	cyclin D2
5	x3120	0.5	8.8	446.4	16q22.1	504	57	D21255_at	1009	D21255	CDH11	cadherin 11 (OB-cadherin, osteoblast)
6	x6580	0.2587	8.9	255.1	1p21	287	32	J04177_at	1301	J04177	COL11A1	collagen, type XI, alpha 1
7	x2140	0.1938	13.3	412.2	8q23	446	33	Y11710_rna1_at	7373	Y11710	COL14A1	collagen, type XIV, alpha 1; undulin
8	x1629	0.2038	8.9	158.8	2p21	179	20	U03688_at	1545	U03688	CYP1B1	cytochrome P450, subfamily I (dioxin-inducible), polypeptide 1 (glaucoma 3, primary infantile)
9	x3108	0.028	13.9	258.1	17p13.1	278	20	U83192_at	1742	U83192	DLG4	discs, large (Drosophila) homolog 4
10	x3342	0.426	6.5	3499.8	5q34	4140	640	X68277_at	1843	X68277	DUSP1	dual specificity phosphatase 1
11	x4985	0.2448	4.4	113.1	8	33	146	U15642_s_at	1875	U15642	E2F5	E2F transcription factor 5, p130-binding
12	x671	0.446	11.2	597.5	4	656	58	D11151_at	1909	D11151	EDNRA	endothelin receptor type A
13	x2341	0.2448	5.5	1078.6	8p21.1	242	1321	HG4535-HT4940_s_at	2039	U28389	EPB49	erythrocyte membrane protein band 4.9 (dematin)
14	x2797	0.0959	25.4	489.0	16p13.3-p13.11	20	509	L76568_xpt3_f_at	2072	L76568	ERCC4	excision repair cross-complementing rodent repair deficiency, complementation group 4
15	x6244	0.3057	3.1	750.5	13q14.1-q14.2	1103	353	M13450_at	2098	M13450	ESD	esterase D/formylglutathione hydrolase
16	x2404	0.2128	8.7	245.1	Xq22	277	32	X97249_at	2491	X97249	FSHPRH1	FSH primary response (LRPR1, rat) homolog 1
17	x4516	0.3247	39.1	761.3	3p21.3	20	781	U49082_at	10991	U49082	G17	G17 transporter protein
18	x4495	0.2218	55.8	3521.2	2p12-q11	3585	64	M85276_at	10578	M85276	GNLY	granulysin
19	x1222	0.014	16.5	310.3	2q14-q21	330	20	M36284_s_at	2995	M36284	GYPC	glycophorin C (Gerbich blood group)
20	x2590	0.1359	7.5	129.1	15q22	149	20	U50078_at	8925	U50078	HERC1	hect (homologous to the E6-AP

												(UBE3A) carboxyl terminus) domain and RCC1 (CHC1)-like domain (RLD) 1
21	x881	0.0599	10.3	185.2	2	205	20	U44111_at	3176	U44111	HNMT	histamine N-methyltransferase
22	x5023	0.2388	11.2	395.1	2q37.1-q36.3	434	39	X77307_at	3357	X77307	HTR2B	5-hydroxytryptamine (serotonin) receptor 2B
23	x2719	0.2108	7.9	206.0	9p22	236	30	J00212_f_at	3452	V00540	IFNA21	interferon, alpha 21
24	x5442	0.1618	42.3	1454.6	12q22-q23	1490	35	X57025_at	3479	X57025	IGF1	insulin-like growth factor 1 (somatomedin C)
25	x5452	0.5	6.2	420.4	19p13.1	501	81	U61263_at	10994	U61263	ILVBL	ilvB (bacterial acetolactate synthase)-like
26	x6197	0.1808	10.4	188.0	4q34.1-q35.1	208	20	X15949_at	3660	X15949	IRF2	interferon regulatory factor 2
27	x3700	0.3447	7.2	124.9	3q21-q25	145	20	D13626_at	9934	D13626	KIAA0001	KIAA0001 gene product
28	x1553	0.1728	3.7	3035.7	12q13	1115	4151	X12876_s_at	3875	X12876	KRT18	keratin 18
29	x5912	0.0669	10.2	4816.8	12q13	521	5338	X74929_s_at	3856	X74929	KRT8	keratin 8
30	x197	0.035	43.7	853.4	16q22.1	873	20	M12625_at	3931	M12625	LCAT	lecithin-cholesterol acyltransferase
31	x723	0.2478	5.8	7378.3	22q13.1	8915	1537	J04456_at	3956	J04456	LGALS1	lectin, galactoside-binding, soluble, 1 (galectin 1)
32	x1271	0.1299	3.8	1609.5	4q	583	2192	M93036_at	4072	M93036	M4S1	membrane component, chromosomal 4, surface marker (35kD glycoprotein)
33	x6752	0.431	4.0	613.2	14	818	205	Z24725_at	10979	Z24725	MIG2	mitogen inducible 2
34	x1469	0.2038	18.2	797.4	14q11-q12	844	46	Z48481_at	4323	Z48481	MMP14	matrix metalloproteinase 14 (membrane-inserted)
35	x879	0.2458	22.3	1149.7	1q43	1204	54	M30269_at	4811	M30269	NID	nidogen (enactin)
36	x1397	0.3946	11.6	724.8	5q14	793	68	HG3510-HT3704_at	7025	X12795	NR2F1	nuclear receptor subfamily 2, group F, member 1
37	x2831	0.2987	6.0	204.3	10q21.3-q23.1	41	245	M24486_s_at	5033	M24486	P4HA1	procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide 1
38	x2670	0.2478	158.2	4966.1	9q34	4998	32	HG721-HT4827_s_at	5047	J04129	PAEP(alt2)	progestagen-associated endometrial protein (placental protein 14, pregnancy-associated endometrial alpha-2-globulin, alpha uterine protein): Alternate Splice 2
39	x5757	0.2038	12.3	3977.7	7q22	4331	353	L33799_at	5118	L33799	PCOLCE	procollagen C-endopeptidase enhancer

40	x6701	0.3077	17.8	1101.4	4q11-q13	1167	65	M21574_at	5156	M21574	PDGFRA	platelet-derived growth factor receptor, alpha polypeptide
41	x6741	0.2068	5.1	120.6	Xq21-q27	150	29	D00860_at	5631	D00860	PRPS1	phosphoribosyl pyrophosphate synthetase 1
42	x1195	0.1099	10.2	183.7	Xp22.3-p22.2	204	20	Y00971_at	5634	Y00971	PRPS2	phosphoribosyl pyrophosphate synthetase 2
43	x5284	0.0789	11.6	212.7	4p15.31	233	20	M16447_at	5860	M16447	QDPR	quinoid dihydropteridine reductase
44	x320	0.4076	5.6	167.7	1p31-p22	204	37	X98001_at	5876	X98001	RABGGTB	Rab geranylgeranyltransferase, beta subunit
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49	x4880	0.038	13.0	239.8	11p13	260	20	X69950_s_at	51352	X69950	WIT-1	Wilms tumor associated protein
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Key:

SEQ ID NO	Sequence identifier number
GeneCode	Internal lab unique identifier, numbers preceded by an "x"
PermaxGPT	Permax value using GPT datastate
FoldGPT	Ratio of NLXGPT to TXGPT, inverted if needed to yield value >1
DeltaGPT	Arithmetic difference of NLXGPT and TXGPT , absolute value
ChrBand	Karyotypic locus of gene
NLXGPT	Mean expression in GPT units of 4 normal endometria
TXGPT	Mean expression in GPT units of 10 endometrioid endometrial adenocarcinomas
AffyProbeSet	Affymetrix probe identifier in HuFL human expression array chip
LocusLink	Locuslink ID number, when available.
GenBank	The GenBank entry for sequence used by Affymetrix to design probes
Abrev	When in full caps, this is the Locuslink recommended nomenclature.
Title	Text description of gene. Usually Locuslink label

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The present invention is not limited in scope by the examples provided, since the examples are intended as illustrations of various aspects of the invention and other functionally equivalent embodiments are within the scope of the invention. Various modifications of the invention in addition to those shown are described herein will become apparent to those skilled in the art for the foregoing description and fall within the scope of the appended claims. The advantages and objects of the invention are not necessarily encompassed by each embodiment of the invention.

All references, patents, and patent publications that are recited in this application are incorporated in their entirety herein by reference.

I claim:

Claims

1. A method for diagnosing endometrial cancer in a subject suspected of having endometrial cancer comprising:

obtaining from the subject an endometrial tissue sample suspected of being cancerous,

determining the expression of a set of nucleic acid molecules or expression products thereof in the endometrial tissue sample, wherein the set of nucleic acid molecules comprises at least two nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

2. The method of claim 1, wherein the set of nucleic acid molecules comprises at least 3 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

3. The method of claim 1, wherein the set includes at least 4 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

4. The method of claim 1, wherein the set includes at least 5 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

5. The method of claim 1, wherein the set includes at least 10 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

6. The method of claim 1, wherein the set includes at least 15 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

7. The method of claim 1, wherein the set includes at least 20 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

8. The method of claim 1, wherein the set includes at least 30 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

9. The method of claim 1, wherein the set includes at least 40 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

10. The method of claim 1, further comprising:

determining the expression of the set of nucleic acid molecules or expression products thereof in a non-cancerous endometrial tissue sample, and comparing the expression of the set of nucleic acid molecules or expression products thereof in the endometrial tissue sample suspected of being cancerous and the non-cancerous endometrial tissue sample.

11. A method for selecting a course of treatment of a subject having or suspected of having endometrial cancer, comprising:

obtaining from the subject an endometrial tissue sample suspected of being cancerous,

determining the expression of a set of nucleic acid markers or expression products thereof which are differentially expressed in endometrial tumor tissue samples, and

selecting a course of treatment appropriate to the endometrial cancer of the subject.

12. The method of claim 11 wherein the endometrial cancer is endometrioid endometrial carcinoma.

13. The method of claim 12, further comprising:

determining the expression of the set of nucleic acid molecules or expression products thereof in a non-cancerous endometrial tissue sample.

14. The method of claim 11, wherein the expression of a set of nucleic acid markers is determined by a method selected from the group consisting of nucleic acid hybridization and nucleic acid amplification.

15. The method of claim 14, wherein the nucleic acid hybridization is performed using a solid-phase nucleic acid molecule array.

16. A method for evaluating treatment of endometrial cancer, comprising:

obtaining a first determination of the expression of a set of nucleic acid molecules, or expression products thereof, which are differentially expressed in an endometrial tumor tissue sample from a subject undergoing treatment for cancer,

obtaining a second determination of the expression of a set of nucleic acid molecules, or expression products thereof, which are differentially expressed in a second endometrial tumor tissue sample from the subject after obtaining the first determination,

comparing the first determination of expression to the second determination of expression as an indication of evaluation of the treatment.

17. The method of claim 16, wherein the cancer is endometrioid endometrial adenocarcinoma.

18. The method of claim 17, further comprising:

determining the expression of a set of nucleic acid markers which are differentially expressed in non-cancerous endometrial tissue samples.

19. The method of claim 16, wherein the expression of a set of nucleic acid markers is determined by a method selected from the group consisting of nucleic acid hybridization and nucleic acid amplification.

20. The method of claim 16, wherein the nucleic acid hybridization is performed using a solid-phase nucleic acid molecule array.

21. A solid-phase nucleic acid molecule array consisting essentially of at least two nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50 fixed to a solid substrate.

22. The solid-phase nucleic acid molecule array of claim 21, further comprising at least one control nucleic acid molecule.

23. The solid-phase nucleic acid molecule array of claim 21, wherein the set of nucleic acid molecules comprises at least 3 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

24. The solid-phase nucleic acid molecule array of claim 21, wherein the set includes at least 4 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

25. The solid-phase nucleic acid molecule array of claim 21, wherein the set includes at least 5 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

26. The solid-phase nucleic acid molecule array of claim 21, wherein the set includes at least 10 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

27. The solid-phase nucleic acid molecule array of claim 21, wherein the set includes at least 15 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

28. The solid-phase nucleic acid molecule array of claim 21, wherein the set includes at least 20 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

29. The solid-phase nucleic acid molecule array of claim 21, wherein the set includes at least 30 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

30. The solid-phase nucleic acid molecule array of claim 21, wherein the set includes at least 40 nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50.

31. The solid-phase nucleic acid molecule array of claim 21, wherein the solid substrate comprises a material selected from the group consisting of glass, silica, aluminosilicates, borosilicates, metal oxides such as alumina and nickel oxide, various clays, nitrocellulose, or nylon.

32. The solid-phase nucleic acid molecule array of claim 21, wherein the nucleic acid molecules are fixed to the solid substrate by covalent bonding.

33. A solid-phase protein microarray comprising at least two antibodies or antigen-binding fragments thereof, that specifically bind at least two different polypeptides selected from the group consisting of SEQ ID NOs:51-100, fixed to a solid substrate.

34. The protein microarray of claim 33, wherein the microarray further comprises an antibody or antigen-binding fragment thereof, that binds specifically to a cancer-associated polypeptide other than those selected from the group consisting of SEQ ID NOs:51-100.

35. The protein microarray of claim 34, wherein the cancer-associated polypeptide other than those selected from the group consisting of SEQ ID NOs: 51-100 is a endometrial cancer associated polypeptide.

36. The protein microarray of claim 33, further comprising at least one control polypeptide molecule.

37. The protein microarray of claim 33, wherein the antibodies are monoclonal or polyclonal antibodies.

38. The protein microarray of claim 33, wherein the antibodies are chimeric, human, or humanized antibodies.

39. The protein microarray of claim 33, wherein the antibodies are single chain antibodies.

40. The protein microarray of claim 33, wherein the antigen-binding fragments are $F(ab')_2$, Fab, Fd, or Fv fragments.

41. A method for identifying lead compounds for a pharmacological agent useful in the treatment of endometrial cancer, comprising:

contacting a endometrial cancer cell or tissue with a candidate pharmacological agent,

determining the expression of a set of nucleic acid molecules in the endometrial cancer cell or tissue sample under conditions which, in the absence of the candidate pharmacological agent, permit a first amount of expression of the set of nucleic acid molecules wherein the set of nucleic acid molecules comprises at least two nucleic acid molecules selected from the group consisting of SEQ ID NOs:1-50, and

detecting a test amount of the expression of the set of nucleic acid molecules, wherein a decrease in the test amount of expression in the presence of the candidate pharmacological

agent relative to the first amount of expression indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which is useful in the treatment of endometrial cancer.

42. The method of claim 41, wherein the set of nucleic acid molecules is differentially expressed in endometrioid endometrial tumor tissue samples.

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ctggtgaacc aataaaagaa ggagataatg actacttcac ttgcataact aaagcttatg 480

aaatgttatc tgatccagtg aaaagacgag catttaacag tgtagatcct acttttgata 540

actcagttcc ttctaaaagt gaagcaaagg ataatttctt cgaagtgttt accccagtgt 600

ttgaaaggaa ttccagatgg tcaaataaaa aaaatgttcc taaacttggt gatatgaatt 660

catcatttga agatgtagat atattttatt ctttctggta taattttgat tcttggagag 720

aattttctta tttagatgaa gaagaaaaag aaaaagcaga atgtcgtgat gagaggagat 780

ggattgaaaa gcagaacgga gcaacaagag cacaaagaaa aaaagaagaa atgaacagaa 840

taagaacatt agttgacaat gcatacagct gtgatccaag gataaaaaag ttcaaggaag 900

aagaaaaagc caagaaagaa gcagaaaaga aagcaaaagc agaagctaaa cggaaggagc 960

aagaagctaa agaaaaacaa agacaagctg aattagaagc tgctcggtta gctaaggaga 1020

aagaagagga ggaagtcaga cagcaagcat tgctggcaaa gaaggaaaaa gatatccaga 1080

aaaaagccat taagaaggaa aggcaaaaac ttcgaaactc atgcaagata gaagaaataa 1140

atgagcaaat cagaaaagag aaagaggaag ctgaggctcg tatgcgacaa gcatctaaga 1200

acacagagaa atcaactggt ggaggtggaa atggaagtaa aaattggtca gaagatgatc 1260

tacaattact aattaaagct gtgaatctgt tccctgctag aacaaattca agatgggaag 1320

ttattgctaa ttacatgaac atacattctt cctctggagt caaaagaact gccaaagatg 1380

ttattggcaa agcaaagagt ctccaaaaac ttgaccctca tcaaaaagat gacataaata 1440

aaaaggcatt tgataagttc aaaaaagaac atggagtggt acctcaagca gacaacgcaa 1500

cgccttcaga acgatttgaa ggtccatata cagacttcac cccttggaca acagaagaac 1560

agaagctttt ggaacaagct ttgaaaacat acccagtaaa tacacctgaa agatgggaaa 1620

aaatagcaga agcggtgcct ggcaggacaa agaaggactg catgaaacga tacaaggaac 1680

ttgtcgagat ggtaaaagca aagaaagctg ctcaagaaca agtgctgaat gcaagtagag 1740

ccaagaaatg acaatctttg ttgtgtgtgc atttttataa taaaactgaa aatactgtaa 1800

acattttcat tcttaaaatt atactcatgg taataatttg aaagtaaaaa aaaaaaaaaa 1860

<210> 51
<211> 729
<212> PRT
<213> Homo sapiens

<400> 51

Met His Leu Lys Ile Val Leu Ala Phe Leu Ala Leu Ser Leu Ile Thr
1 5 10 15

Ile Phe Ala Leu Ala Tyr Val Leu Leu Thr Ser Pro Gly Gly Ser Ser
20 25 30

Gln Pro Pro His Cys Pro Ser Val Ser His Arg Ala Gln Pro Trp Pro
35 40 45

His Pro Gly Gln Ser Gln Leu Phe Ala Asp Leu Ser Arg Glu Glu Leu
50 55 60

Thr Ala Val Met Arg Phe Leu Thr Gln Arg Leu Gly Pro Gly Leu Val
65 70 75 80

Asp Ala Ala Gln Ala Gln Pro Ser Asp Asn Cys Ile Phe Ser Val Glu
85 90 95

Leu Gln Leu Pro Pro Lys Ala Ala Ala Leu Ala His Leu Asp Arg Gly
100 105 110

Ser Pro Pro Pro Ala Arg Glu Ala Leu Ala Ile Val Leu Phe Gly Gly
115 120 125

Gln Pro Gln Pro Asn Val Ser Glu Leu Val Val Gly Pro Leu Pro His
130 135 140

Pro Ser Tyr Met Arg Asp Val Thr Val Glu Arg His Gly Gly Pro Leu
145 150 155 160

Pro Tyr His Arg Arg Pro Val Leu Arg Ala Glu Phe Thr Gln Met Trp
165 170 175

Arg His Leu Lys Asp Val Glu Leu Pro Lys Ala Pro Ile Phe Leu Ser
180 185 190

Ser Thr Phe Asn Tyr Asn Gly Ser Thr Leu Ala Ala Val His Ala Thr
195 200 205

Pro Arg Gly Leu Arg Ser Arg Glu Arg Thr Thr Trp Ile Gly Leu Tyr
210 215 220

His Asn Ile Ser Gly Val Gly Leu Phe Leu His Pro Val Gly Leu Glu
225 230 235 240

Leu Leu Leu Asp His Arg Ala Leu Asp Pro Ala His Trp Thr Val Gln
245 250 255

Gln Val Phe Tyr Leu Gly His Tyr Tyr Ala Asp Leu Gly Gln Leu Glu
260 265 270

Arg Glu Phe Lys Ser Gly Arg Leu Glu Val Val Arg Val Pro Leu Pro
275 280 285

Pro Pro Asn Gly Ala Ser Ser Leu Arg Ser Arg Asn Ser Pro Gly Pro
290 295 300

Leu Pro Pro Leu Gln Phe Ser Pro Gln Gly Ser Gln Tyr Ser Val Gln
305 310 315 320

Gly Asn Leu Val Val Ser Ser Leu Trp Ser Phe Thr Phe Gly His Gly
325 330 335

Val Phe Ser Gly Leu Arg Ile Phe Asp Val Arg Phe Gln Gly Glu Arg
340 345 350

Ile Ala Tyr Glu Val Ser Val Gln Glu Cys Val Ser Ile Tyr Gly Ala
355 360 365

Asp Ser Pro Lys Thr Met Leu Thr Arg Tyr Leu Asp Ser Ser Phe Gly
370 375 380

Leu Gly Arg Asn Ser Arg Gly Leu Val Arg Gly Val Asp Cys Pro Tyr
385 390 395 400

Gln Ala Thr Met Val Asp Ile His Ile Leu Val Gly Lys Gly Ala Val
405 410 415

Gln Leu Leu Pro Gly Ala Val Cys Val Phe Glu Glu Ala Gln Gly Leu
420 425 430

Pro Leu Arg Arg His His Asn Tyr Leu Gln Asn His Phe Tyr Gly Gly
435 440 445

Leu Ala Ser Ser Ala Leu Val Val Arg Ser Val Ser Ser Val Gly Asn
450 455 460

Tyr Asp Tyr Ile Trp Asp Phe Val Leu Tyr Pro Asn Gly Ala Leu Glu
465 470 475 480

Gly Arg Val His Ala Thr Gly Tyr Ile Asn Thr Ala Phe Leu Lys Gly
485 490 495

Gly Glu Glu Gly Leu Leu Phe Gly Asn Arg Val Gly Glu Arg Val Leu
500 505 510

Gly Thr Val His Thr His Ala Phe His Phe Lys Leu Asp Leu Asp Val
515 520 525

Ala Gly Leu Lys Asn Trp Val Val Ala Glu Asp Val Val Phe Lys Pro
530 535 540

Val Ala Ala Pro Trp Asn Pro Glu His Trp Leu Gln Arg Pro Gln Leu
545 550 555 560

Thr Arg Gln Val Leu Gly Lys Glu Asp Leu Thr Ala Phe Ser Leu Gly
565 570 575

Ser Pro Leu Pro Arg Tyr Leu Tyr Leu Ala Ser Asn Gln Thr Asn Ala
580 585 590

Trp Gly His Gln Arg Gly Tyr Gln Leu Val Val Thr Gln Arg Lys Glu
595 600 605

Glu Glu Ser Gln Ser Ser Ser Ile Tyr His Gln Asn Asp Ile Trp Thr
610 615 620

Pro Thr Val Thr Phe Ala Asp Phe Ile Asn Asn Glu Thr Leu Leu Gly
625 630 635 640

Glu Asp Leu Val Ala Trp Val Thr Ala Ser Phe Leu His Ile Pro His
645 650 655

Ala Glu Asp Ile Pro Asn Thr Val Thr Leu Gly Asn Arg Val Gly Phe
660 665 670

Leu Leu Arg Pro Tyr Asn Phe Phe Asp Glu Asp Pro Ser Ile Phe Ser
675 680 685

Pro Gly Ser Val Tyr Phe Glu Lys Gly Gln Asp Ala Gly Leu Cys Ser
690 695 700

Ile Asn Pro Val Ala Cys Leu Pro Asp Leu Ala Ala Cys Val Pro Asp
705 710 715 720

Leu Pro Pro Phe Ser Tyr His Gly Phe
725

<210> 52
<211> 885
<212> PRT
<213> Homo sapiens

<400> 52

Met Ala Trp Arg Cys Pro Arg Met Gly Arg Val Pro Leu Ala Trp Cys
1 5 10 15

Leu Ala Leu Cys Gly Trp Ala Cys Met Ala Pro Arg Gly Thr Gln Ala
20 25 30

Glu Glu Ser Pro Phe Val Gly Asn Pro Gly Asn Ile Thr Gly Ala Arg
35 40 45

Gly Leu Thr Gly Thr Leu Arg Cys Gln Leu Gln Val Gln Gly Glu Pro
50 55 60

Pro Glu Val His Trp Leu Arg Asp Gly Gln Ile Leu Glu Leu Ala Asp
65 70 75 80

Ser Thr Gln Thr Gln Val Pro Leu Gly Glu Asp Glu Gln Asp Asp Trp
85 90 95

Ile Val Val Ser Gln Leu Arg Ile Thr Ser Leu Gln Leu Ser Asp Thr
100 105 110

Gly Gln Tyr Gln Cys Leu Val Phe Leu Gly His Gln Thr Phe Val Ser
115 120 125

Gln Pro Gly Tyr Val Gly Leu Glu Gly Leu Pro Tyr Phe Leu Glu Glu
130 135 140

Pro Glu Asp Arg Thr Val Ala Ala Asn Thr Pro Phe Asn Leu Ser Cys
145 150 155 160

Gln Ala Gln Gly Pro Pro Glu Pro Val Asp Leu Leu Trp Leu Gln Asp
165 170 175

Ala Val Pro Leu Ala Thr Ala Pro Gly His Gly Pro Gln Arg Ser Leu
180 185 190

His Val Pro Gly Leu Asn Lys Thr Ser Ser Phe Ser Cys Glu Ala His
195 200 205

Asn Ala Lys Gly Val Thr Thr Ser Arg Thr Ala Thr Ile Thr Val Leu
210 215 220

Pro Gln Gln Pro Arg Asn Leu His Leu Val Ser Arg Gln Pro Thr Glu
225 230 235 240

Leu Glu Val Ala Trp Thr Pro Gly Leu Ser Gly Ile Tyr Pro Leu Thr
245 250 255

His Cys Thr Leu Gln Ala Val Leu Ser Asp Asp Gly Met Gly Ile Gln
260 265 270

Ala Gly Glu Pro Asp Pro Pro Glu Glu Pro Leu Thr Ser Gln Ala Ser
275 280 285

Val Pro Pro His Gln Leu Arg Leu Gly Ser Leu His Pro His Thr Pro
290 295 300

Tyr His Ile Arg Val Ala Cys Thr Ser Ser Gln Gly Pro Ser Ser Trp
305 310 315 320

Thr His Trp Leu Pro Val Glu Thr Pro Glu Gly Val Pro Leu Gly Pro
325 330 335

Pro Lys Asn Ile Ser Ala Thr Arg Asn Gly Ser Gln Ala Phe Val His
340 345 350

Trp Gln Glu Pro Arg Ala Pro Leu Gln Gly Thr Leu Leu Gly Tyr Arg
355 360 365

Leu Ala Tyr Gln Gly Gln Asp Thr Pro Glu Val Leu Met Asp Ile Gly
370 375 380

Leu Arg Gln Glu Val Thr Leu Glu Leu Gln Gly Asp Gly Ser Val Ser
385 390 395 400

Asn Leu Thr Val Cys Val Ala Ala Tyr Thr Ala Ala Gly Asp Gly Pro
405 410 415

Trp Ser Leu Pro Val Pro Leu Glu Ala Trp Arg Pro Val Lys Glu Pro
420 425 430

Ser Thr Pro Ala Phe Ser Trp Pro Trp Trp Tyr Val Leu Leu Gly Ala
435 440 445

Val Val Ala Ala Ala Cys Val Leu Ile Leu Ala Leu Phe Leu Val His
450 455 460

Arg Arg Lys Lys Glu Thr Arg Tyr Gly Glu Val Phe Glu Pro Thr Val
465 470 475 480

Glu Arg Gly Glu Leu Val Val Arg Tyr Arg Val Arg Lys Ser Tyr Ser
485 490 495

Arg Arg Thr Thr Glu Ala Thr Leu Asn Ser Leu Gly Ile Ser Glu Glu
500 505 510

Leu Lys Glu Lys Leu Arg Asp Val Met Val Asp Arg His Lys Val Ala
515 520 525

Leu Gly Lys Thr Leu Gly Glu Gly Glu Phe Gly Ala Val Met Glu Gly
530 535 540

Gln Leu Asn Gln Asp Asp Ser Ile Leu Lys Val Ala Val Lys Thr Met
545 550 555 560

Lys Ile Ala Ile Cys Thr Arg Ser Glu Leu Glu Asp Phe Leu Ser Glu
565 570 575

Ala Val Cys Met Lys Glu Phe Asp His Pro Asn Val Met Arg Leu Ile
580 585 590

Gly Val Cys Phe Gln Gly Ser Glu Arg Glu Ser Phe Pro Ala Pro Val
595 600 605

Val Ile Leu Pro Phe Met Lys His Gly Asp Leu His Ser Phe Leu Leu
610 615 620

Tyr Ser Arg Leu Gly Asp Gln Pro Val Tyr Leu Pro Thr Gln Met Leu
625 630 635 640

Val Lys Phe Met Ala Asp Ile Ala Ser Gly Met Glu Tyr Leu Ser Thr
645 650 655

Lys Arg Phe Ile His Arg Asp Leu Ala Ala Arg Asn Cys Met Leu Asn
660 665 670

Glu Asn Met Ser Val Cys Val Ala Asp Phe Gly Leu Ser Lys Lys Ile
675 680 685

Tyr Asn Gly Asp Tyr Tyr Arg Gln Gly Arg Ile Ala Lys Met Pro Val
690 695 700

Lys Trp Ile Ala Ile Glu Ser Leu Ala Asp Arg Val Tyr Thr Ser Lys
705 710 715 720

Ser Asp Val Trp Ser Phe Gly Val Thr Met Trp Glu Ile Ala Thr Arg
725 730 735

Gly Gln Thr Pro Tyr Pro Gly Val Glu Asn Ser Glu Ile Tyr Asp Tyr
740 745 750

Leu Arg Gln Gly Asn Arg Leu Lys Gln Pro Ala Asp Cys Leu Asp Gly
755 760 765

Leu Tyr Ala Leu Met Ser Arg Cys Trp Glu Leu Asn Pro Gln Asp Arg
770 775 780

Pro Ser Phe Thr Glu Leu Arg Glu Asp Leu Glu Asn Thr Leu Lys Ala
785 790 795 800

Leu Pro Pro Ala Gln Glu Pro Asp Glu Ile Leu Tyr Val Asn Met Asp
805 810 815

Glu Gly Gly Gly Tyr Pro Glu Pro Pro Gly Ala Ala Gly Gly Ala Asp
820 825 830

Pro Pro Thr Gln Pro Asp Pro Lys Asp Ser Cys Ser Cys Leu Thr Ala
835 840 845

Ala Glu Val His Pro Ala Gly Arg Tyr Val Leu Cys Pro Ser Thr Thr
850 855 860

Pro Ser Pro Ala Gln Pro Ala Asp Arg Gly Ser Pro Ala Ala Pro Gly
865 870 875 880

Gln Glu Asp Gly Ala
885

<210> 53
<211> 373
<212> PRT
<213> Homo sapiens

<400> 53

Met Leu Leu Gly Leu Ala Ala Met Glu Leu Lys Val Trp Val Asp Gly
1 5 10 15

Ile Gln Arg Val Val Cys Gly Val Ser Glu Gln Thr Thr Cys Gln Glu
20 25 30

Val Val Ile Ala Leu Ala Gln Ala Ile Gly Gln Thr Gly Arg Phe Val
35 40 45

Leu Val Gln Arg Leu Arg Glu Lys Glu Arg Gln Leu Leu Pro Gln Glu
50 55 60

Cys Pro Val Gly Ala Gln Ala Thr Cys Gly Gln Phe Ala Ser Asp Val
65 70 75 80

Gln Phe Val Leu Arg Arg Thr Gly Pro Ser Leu Ala Gly Arg Pro Ser
85 90 95

Ser Asp Ser Cys Pro Pro Pro Glu Arg Cys Leu Ile Arg Ala Ser Leu
100 105 110

Pro Val Lys Pro Arg Ala Ala Leu Gly Cys Glu Pro Arg Lys Thr Leu
115 120 125

Thr Pro Glu Pro Ala Pro Ser Leu Ser Arg Pro Gly Pro Ala Ala Pro
130 135 140

Val Thr Pro Thr Pro Gly Cys Cys Thr Asp Leu Arg Gly Leu Glu Leu
145 150 155 160

Arg Val Gln Arg Asn Ala Glu Glu Leu Gly His Glu Ala Phe Trp Glu
165 170 175

Gln Glu Leu Arg Arg Glu Gln Ala Arg Glu Arg Glu Gly Gln Ala Arg
180 185 190

Leu Gln Ala Leu Ser Ala Ala Thr Ala Glu His Ala Ala Arg Leu Gln
195 200 205

Ala Leu Asp Ala Gln Ala Arg Ala Leu Glu Ala Glu Leu Gln Leu Ala
210 215 220

Ala Glu Ala Pro Gly Pro Pro Ser Pro Met Ala Ser Ala Thr Glu Arg
225 230 235 240

Leu His Gln Asp Leu Ala Val Gln Glu Arg Gln Ser Ala Glu Val Gln
245 250 255

Gly Ser Leu Ala Leu Val Ser Arg Ala Leu Glu Ala Ala Glu Arg Ala
260 265 270

Leu Gln Ala Gln Ala Gln Glu Leu Glu Glu Leu Asn Arg Glu Leu Arg

275 280 285

Gln Cys Asn Leu Gln Gln Phe Ile Gln Gln Thr Gly Ala Ala Leu Pro
290 295 300

Pro Pro Pro Arg Pro Asp Arg Gly Pro Pro Gly Thr Gln Gly Pro Leu
305 310 315 320

Pro Pro Ala Arg Glu Glu Ser Leu Leu Gly Ala Pro Ser Glu Ser His
325 330 335

Ala Gly Ala Gln Pro Arg Pro Arg Gly Gly Pro His Asp Ala Glu Leu
340 345 350

Leu Glu Val Ala Ala Ala Pro Ala Pro Glu Trp Cys Pro Leu Ala Ala
355 360 365

Gln Pro Gln Ala Leu
370

<210> 54
<211> 289
<212> PRT
<213> Homo sapiens

<400> 54

Met Glu Leu Leu Cys His Glu Val Asp Pro Val Arg Arg Ala Val Arg
1 5 10 15

Asp Arg Asn Leu Leu Arg Asp Asp Arg Val Leu Gln Asn Leu Leu Thr
20 25 30

Ile Glu Glu Arg Tyr Leu Pro Gln Cys Ser Tyr Phe Lys Cys Val Gln
35 40 45

Lys Asp Ile Gln Pro Tyr Met Arg Arg Met Val Ala Thr Trp Met Leu
50 55 60

Glu Val Cys Glu Glu Gln Lys Cys Glu Glu Glu Val Phe Pro Leu Ala
65 70 75 80

Met Asn Tyr Leu Asp Arg Phe Leu Ala Gly Val Pro Thr Pro Lys Ser
85 90 95

His Leu Gln Leu Leu Gly Ala Val Cys Met Phe Leu Ala Ser Lys Leu
100 105 110

Lys Glu Thr Ser Pro Leu Thr Ala Glu Lys Leu Cys Ile Tyr Thr Asp
115 120 125

Asn Ser Ile Lys Pro Gln Glu Leu Leu Glu Trp Glu Leu Val Val Leu
130 135 140

Gly Lys Leu Lys Trp Asn Leu Ala Ala Val Thr Pro His Asp Phe Ile
145 150 155 160

Glu His Ile Leu Arg Lys Leu Pro Gln Gln Arg Glu Lys Leu Ser Leu
165 170 175

Ile Arg Lys His Ala Gln Thr Phe Ile Ala Leu Cys Ala Thr Asp Phe
180 185 190

Lys Phe Ala Met Tyr Pro Pro Ser Met Ile Ala Thr Gly Ser Val Gly
195 200 205

Ala Ala Ile Cys Gly Leu Gln Gln Asp Glu Glu Val Ser Ser Leu Thr
210 215 220

Cys Asp Ala Leu Thr Glu Leu Leu Ala Lys Ile Thr Asn Thr Asp Val
225 230 235 240

Asp Cys Leu Lys Ala Cys Gln Glu Gln Ile Glu Ala Val Leu Leu Asn
245 250 255

Ser Leu Gln Gln Tyr Arg Gln Asp Gln Arg Asp Gly Ser Lys Ser Glu
260 265 270

Asp Glu Leu Asp Gln Ala Ser Thr Pro Thr Asp Val Arg Asp Ile Asp
275 280 285

Leu

<210> 55
<211> 693
<212> PRT
<213> Homo sapiens

<400> 55

Met Lys Glu Asn Tyr Cys Leu Gln Ala Ala Leu Val Cys Leu Gly Met
1 5 10 15

Leu Cys His Ser His Ala Phe Ala Pro Glu Arg Arg Gly His Leu Arg
20 25 30

Pro Ser Phe His Gly His His Glu Lys Gly Lys Glu Gly Gln Val Leu
35 40 45

Gln Arg Ser Lys Arg Gly Trp Val Trp Asn Gln Phe Phe Val Ile Glu
50 55 60

Glu Tyr Thr Gly Pro Asp Pro Val Leu Val Gly Arg Leu His Ser Asp
65 70 75 80

Ile Asp Ser Gly Asp Gly Asn Ile Lys Tyr Ile Leu Ser Gly Glu Gly
85 90 95

Ala Gly Thr Ile Phe Val Ile Asp Asp Lys Ser Gly Asn Ile His Ala
100 105 110

Thr Lys Thr Leu Asp Arg Glu Glu Arg Ala Gln Tyr Thr Leu Met Ala
115 120 125

Gln Ala Val Asp Arg Asp Thr Asn Arg Pro Leu Glu Pro Pro Ser Glu
130 135 140

Phe Ile Val Lys Val Gln Asp Ile Asn Asp Asn Pro Pro Glu Phe Leu
145 150 155 160

```
His Glu Thr Tyr His Ala Asn Val Pro Glu Arg Ser Asn Val Gly Thr
                  165                 170                 175

Ser Val Ile Gln Val Thr Ala Ser Asp Ala Asp Asp Pro Thr Tyr Gly
             180                 185                 190

Asn Ser Ala Lys Leu Val Tyr Ser Ile Leu Glu Gly Gln Pro Tyr Phe
         195                 200                 205

Ser Val Glu Ala Gln Thr Gly Ile Ile Arg Thr Ala Leu Pro Asn Met
     210                 215                 220

Asp Arg Glu Ala Lys Glu Glu Tyr His Val Val Ile Gln Ala Lys Asp
225                 230                 235                 240

Met Gly Gly His Met Gly Gly Leu Ser Gly Thr Thr Lys Val Thr Ile
                  245                 250                 255

Thr Leu Thr Asp Val Asn Asp Asn Pro Pro Lys Phe Pro Gln Ser Val
             260                 265                 270

Tyr Gln Ile Ser Val Ser Glu Ala Ala Val Pro Gly Glu Glu Val Gly
         275                 280                 285

Arg Val Lys Ala Lys Asp Pro Asp Ile Gly Glu Asn Gly Leu Val Thr
     290                 295                 300

Tyr Asn Ile Val Asp Gly Asp Gly Met Glu Ser Phe Glu Ile Thr Thr
305                 310                 315                 320

Asp Tyr Glu Thr Gln Glu Gly Val Ile Lys Leu Lys Lys Pro Val Asp
                  325                 330                 335

Phe Glu Thr Lys Arg Ala Tyr Ser Leu Lys Val Glu Ala Ala Asn Val
             340                 345                 350

His Ile Asp Pro Lys Phe Ile Ser Asn Gly Pro Phe Lys Asp Thr Val
         355                 360                 365

Thr Val Lys Ile Ala Val Glu Asp Ala Asp Glu Pro Pro Met Phe Leu
     370                 375                 380

Ala Pro Ser Tyr Ile His Glu Val Gln Glu Asn Ala Ala Ala Gly Thr
385                 390                 395                 400

Val Val Gly Arg Val His Ala Lys Asp Pro Asp Ala Ala Asn Ser Pro
                  405                 410                 415

Ile Arg Tyr Ser Ile Asp Arg His Thr Asp Leu Asp Arg Phe Phe Thr
             420                 425                 430

Ile Asn Pro Glu Asp Gly Phe Ile Lys Thr Thr Lys Pro Leu Asp Arg
         435                 440                 445

Glu Glu Thr Ala Trp Leu Asn Ile Thr Val Phe Ala Ala Glu Ile His
     450                 455                 460

Asn Arg His Gln Glu Ala Lys Val Pro Val Ala Ile Arg Val Leu Asp
465                 470                 475                 480
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Val Asn Asp Asn Ala Pro Lys Phe Ala Ala Pro Tyr Glu Gly Phe Ile
485 490 495

Cys Glu Ser Asp Gln Thr Lys Pro Leu Ser Asn Gln Pro Ile Val Thr
500 505 510

Ile Ser Ala Asp Asp Lys Asp Asp Thr Ala Asn Gly Pro Arg Phe Ile
515 520 525

Phe Ser Leu Pro Pro Glu Ile Ile His Asn Pro Asn Phe Thr Val Arg
530 535 540

Asp Asn Arg Asp Asn Thr Ala Gly Val Tyr Ala Arg Arg Gly Gly Phe
545 550 555 560

Ser Arg Gln Lys Gln Asp Leu Tyr Leu Leu Pro Ile Val Ile Ser Asp
565 570 575

Gly Gly Ile Pro Pro Met Ser Ser Thr Asn Thr Leu Thr Ile Lys Val
580 585 590

Cys Gly Cys Asp Val Asn Gly Ala Leu Leu Ser Cys Asn Ala Glu Ala
595 600 605

Tyr Ile Leu Asn Ala Gly Leu Ser Thr Gly Ala Leu Ile Ala Ile Leu
610 615 620

Ala Cys Ile Val Ile Leu Leu Gly Cys Pro Ser Leu Met Glu Pro Pro
625 630 635 640

Ser Pro Arg Glu Asp Met Arg Leu Leu Tyr Leu Gly Phe Gln Leu Met
645 650 655

Leu Phe Ser Tyr Val Lys Val Asn Arg Arg Phe Cys Leu Leu Gly Val
660 665 670

Phe Ile Lys Leu Pro Phe Leu Tyr Val Val Ala Thr Glu Ser Pro Thr
675 680 685

Thr Leu Thr Ser Leu
690

<210> 56
<211> 1806
<212> PRT
<213> Homo sapiens

<220>
<221> UNSURE
<222> (758)..(758)
<223> Xaa = any amino acid

<220>
<221> UNSURE
<222> (809)..(809)
<223> Xaa = any amino acid

<400> 56

Met Glu Pro Trp Ser Ser Arg Trp Lys Thr Lys Arg Trp Leu Trp Asp
1 5 10 15

Phe Thr Val Thr Thr Leu Ala Leu Thr Phe Leu Phe Gln Ala Arg Glu
20 25 30

Val Arg Gly Ala Ala Pro Val Asp Val Leu Lys Ala Leu Asp Phe His
35 40 45

Asn Ser Pro Glu Gly Ile Ser Lys Thr Thr Gly Phe Cys Thr Asn Arg
50 55 60

Lys Asn Ser Lys Gly Ser Asp Thr Ala Tyr Arg Val Ser Lys Gln Ala
65 70 75 80

Gln Leu Ser Ala Pro Thr Lys Gln Leu Phe Pro Gly Gly Thr Phe Pro
85 90 95

Glu Asp Phe Ser Ile Leu Phe Thr Val Lys Pro Lys Lys Gly Ile Gln
100 105 110

Ser Phe Leu Leu Ser Ile Tyr Asn Glu His Gly Ile Gln Gln Ile Gly
115 120 125

Val Glu Val Gly Arg Ser Pro Val Phe Leu Phe Glu Asp His Thr Gly
130 135 140

Lys Pro Ala Pro Glu Asp Tyr Pro Leu Phe Arg Thr Val Asn Ile Ala
145 150 155 160

Asp Gly Lys Trp His Arg Val Ala Ile Ser Val Glu Lys Lys Thr Val
165 170 175

Thr Met Ile Val Asp Cys Lys Lys Lys Thr Thr Lys Pro Leu Asp Arg
180 185 190

Ser Glu Arg Ala Ile Val Asp Thr Asn Gly Ile Thr Val Phe Gly Thr
195 200 205

Arg Ile Leu Asp Glu Glu Val Phe Glu Gly Asp Ile Gln Gln Phe Leu
210 215 220

Ile Thr Gly Asp Pro Lys Ala Ala Tyr Asp Tyr Cys Glu His Tyr Ser
225 230 235 240

Pro Asp Cys Asp Ser Ser Ala Pro Lys Ala Ala Gln Ala Gln Glu Pro
245 250 255

Gln Ile Asp Glu Tyr Ala Pro Glu Asp Ile Ile Glu Tyr Asp Tyr Glu
260 265 270

Tyr Gly Glu Ala Glu Tyr Lys Glu Ala Glu Ser Val Thr Glu Gly Pro
275 280 285

Thr Val Thr Glu Glu Thr Ile Ala Gln Thr Glu Ala Asn Ile Val Asp
290 295 300

Asp Phe Gln Glu Tyr Asn Tyr Gly Thr Met Glu Ser Tyr Gln Thr Glu

305 310 315 320

Ala Pro Arg His Val Ser Gly Thr Asn Glu Pro Asn Pro Val Glu Glu
325 330 335

Ile Phe Thr Glu Glu Tyr Leu Thr Gly Glu Asp Tyr Asp Ser Gln Arg
340 345 350

Lys Asn Ser Glu Asp Thr Leu Tyr Glu Asn Lys Glu Ile Asp Gly Arg
355 360 365

Asp Ser Asp Leu Leu Val Asp Gly Asp Leu Gly Glu Tyr Asp Phe Tyr
370 375 380

Glu Tyr Lys Glu Tyr Glu Asp Lys Pro Thr Ser Pro Pro Asn Glu Glu
385 390 395 400

Phe Gly Pro Gly Val Pro Ala Glu Thr Asp Ile Thr Glu Thr Ser Ile
405 410 415

Asn Gly His Gly Ala Tyr Gly Glu Lys Gly Gln Lys Gly Glu Pro Ala
420 425 430

Val Val Glu Pro Gly Met Leu Val Glu Gly Pro Pro Gly Pro Ala Gly
435 440 445

Pro Ala Gly Ile Met Gly Pro Pro Gly Leu Gln Gly Pro Thr Gly Pro
450 455 460

Pro Gly Asp Pro Gly Asp Arg Gly Pro Pro Gly Arg Pro Gly Leu Pro
465 470 475 480

Gly Ala Asp Gly Leu Pro Gly Pro Pro Gly Thr Met Leu Met Leu Pro
485 490 495

Phe Arg Tyr Gly Gly Asp Gly Ser Lys Gly Pro Thr Ile Ser Ala Gln
500 505 510

Glu Ala Gln Ala Gln Ala Ile Leu Gln Gln Ala Arg Ile Ala Leu Arg
515 520 525

Gly Pro Pro Gly Pro Met Gly Leu Thr Gly Arg Pro Gly Pro Val Gly
530 535 540

Gly Pro Gly Ser Ser Gly Ala Lys Gly Glu Ser Gly Asp Pro Gly Pro
545 550 555 560

Gln Gly Pro Arg Gly Val Gln Gly Pro Pro Gly Pro Thr Gly Lys Pro
565 570 575

Gly Lys Arg Gly Arg Pro Gly Ala Asp Gly Gly Arg Gly Met Pro Gly
580 585 590

Glu Pro Gly Ala Lys Gly Asp Arg Gly Phe Asp Gly Leu Pro Gly Leu
595 600 605

Pro Gly Asp Lys Gly His Arg Gly Glu Arg Gly Pro Gln Gly Pro Pro
610 615 620

Gly Pro Pro Gly Asp Asp Gly Met Arg Gly Glu Asp Gly Glu Ile Gly

625 630 635 640

Pro Arg Gly Leu Pro Gly Glu Ala Gly Pro Arg Gly Leu Leu Gly Pro
645 650 655

Arg Gly Thr Pro Gly Ala Pro Gly Gln Pro Gly Met Ala Gly Val Asp
660 665 670

Gly Pro Pro Gly Pro Lys Gly Asn Met Gly Pro Gln Gly Glu Pro Gly
675 680 685

Pro Pro Gly Gln Gln Gly Asn Pro Gly Pro Gln Gly Leu Pro Gly Pro
690 695 700

Gln Gly Pro Ile Gly Pro Pro Gly Glu Lys Gly Pro Gln Gly Lys Pro
705 710 715 720

Gly Leu Ala Gly Leu Pro Gly Ala Asp Gly Pro Pro Gly His Pro Gly
725 730 735

Lys Glu Gly Gln Ser Gly Glu Lys Gly Ala Leu Gly Pro Pro Gly Pro
740 745 750

Gln Gly Pro Ile Gly Xaa Pro Gly Pro Arg Gly Val Lys Gly Ala Asp
755 760 765

Gly Val Arg Gly Leu Lys Gly Ser Lys Gly Glu Lys Gly Glu Asp Gly
770 775 780

Phe Pro Gly Phe Lys Gly Asp Met Gly Leu Lys Gly Asp Arg Gly Glu
785 790 795 800

Val Gly Gln Ile Gly Pro Arg Gly Xaa Asp Gly Pro Glu Gly Pro Lys
805 810 815

Gly Arg Ala Gly Pro Thr Gly Asp Pro Gly Pro Ser Gly Gln Ala Gly
820 825 830

Glu Lys Gly Lys Leu Gly Val Pro Gly Leu Pro Gly Tyr Pro Gly Arg
835 840 845

Gln Gly Pro Lys Gly Ser Thr Gly Phe Pro Gly Phe Pro Gly Ala Asn
850 855 860

Gly Glu Lys Gly Ala Arg Gly Val Ala Gly Lys Pro Gly Pro Arg Gly
865 870 875 880

Gln Arg Gly Pro Thr Gly Pro Arg Gly Ser Arg Gly Ala Arg Gly Pro
885 890 895

Thr Gly Lys Pro Gly Pro Lys Gly Thr Ser Gly Gly Asp Gly Pro Pro
900 905 910

Gly Pro Pro Gly Glu Arg Gly Pro Gln Gly Pro Gln Gly Pro Val Gly
915 920 925

Phe Pro Gly Pro Lys Gly Pro Pro Gly Pro Pro Gly Arg Met Gly Cys
930 935 940

Pro Gly His Pro Gly Gln Arg Gly Glu Thr Gly Phe Gln Gly Lys Thr

945 950 955 960

Gly Pro Pro Gly Pro Gly Gly Val Val Gly Pro Gln Gly Pro Thr Gly
965 970 975

Glu Thr Gly Pro Ile Gly Glu Arg Gly Tyr Pro Gly Pro Pro Gly Pro
980 985 990

Pro Gly Glu Gln Gly Leu Pro Gly Ala Ala Gly Lys Glu Gly Ala Lys
995 1000 1005

Gly Asp Pro Gly Pro Gln Gly Ile Ser Gly Lys Asp Gly Pro Ala
1010 1015 1020

Gly Leu Arg Gly Phe Pro Gly Glu Arg Gly Leu Pro Gly Ala Gln
1025 1030 1035

Gly Ala Pro Gly Leu Lys Gly Gly Glu Gly Pro Gln Gly Pro Pro
1040 1045 1050

Gly Pro Val Gly Ser Pro Gly Glu Arg Gly Ser Ala Gly Thr Ala
1055 1060 1065

Gly Pro Ile Gly Leu Arg Gly Arg Pro Gly Pro Gln Gly Pro Pro
1070 1075 1080

Gly Pro Ala Gly Glu Lys Gly Ala Pro Gly Glu Lys Gly Pro Gln
1085 1090 1095

Gly Pro Ala Gly Arg Asp Gly Val Gln Gly Pro Val Gly Leu Pro
1100 1105 1110

Gly Pro Ala Gly Pro Ala Gly Ser Pro Gly Glu Asp Gly Asp Lys
1115 1120 1125

Gly Glu Ile Gly Glu Pro Gly Gln Lys Gly Ser Lys Gly Gly Lys
1130 1135 1140

Gly Glu Asn Gly Pro Pro Gly Pro Pro Gly Leu Gln Gly Pro Val
1145 1150 1155

Gly Ala Pro Gly Ile Ala Gly Gly Asp Gly Glu Pro Gly Pro Arg
1160 1165 1170

Gly Gln Gln Gly Met Phe Gly Gln Lys Gly Asp Glu Gly Ala Arg
1175 1180 1185

Gly Phe Pro Gly Pro Pro Gly Pro Ile Gly Leu Gln Gly Leu Pro
1190 1195 1200

Gly Pro Pro Gly Glu Lys Gly Glu Asn Gly Asp Val Gly Pro Trp
1205 1210 1215

Gly Pro Pro Gly Pro Pro Gly Pro Arg Gly Pro Gln Gly Pro Asn
1220 1225 1230

Gly Ala Asp Gly Pro Gln Gly Pro Pro Gly Ser Val Gly Ser Val
1235 1240 1245

Gly Gly Val Gly Glu Lys Gly Glu Pro Gly Glu Ala Gly Asn Pro

1250 1255 1260

Gly Pro Pro Gly Glu Ala Gly Val Gly Gly Pro Lys Gly Glu Arg
1265 1270 1275

Gly Glu Lys Gly Glu Ala Gly Pro Pro Gly Ala Ala Gly Pro Pro
1280 1285 1290

Gly Ala Lys Gly Pro Pro Gly Asp Asp Gly Pro Lys Gly Asn Pro
1295 1300 1305

Gly Pro Val Gly Phe Pro Gly Asp Pro Gly Pro Pro Gly Glu Leu
1310 1315 1320

Gly Pro Ala Gly Gln Asp Gly Val Gly Gly Asp Lys Gly Glu Asp
1325 1330 1335

Gly Asp Pro Gly Gln Pro Gly Pro Pro Gly Pro Ser Gly Glu Ala
1340 1345 1350

Gly Pro Pro Gly Pro Pro Gly Lys Arg Gly Pro Pro Gly Ala Ala
1355 1360 1365

Gly Ala Glu Gly Arg Gln Gly Glu Lys Gly Ala Lys Gly Glu Ala
1370 1375 1380

Gly Ala Glu Gly Pro Pro Gly Lys Thr Gly Pro Val Gly Pro Gln
1385 1390 1395

Gly Pro Ala Gly Lys Pro Gly Pro Glu Gly Leu Arg Gly Ile Pro
1400 1405 1410

Gly Pro Val Gly Glu Gln Gly Leu Pro Gly Ala Ala Gly Gln Asp
1415 1420 1425

Gly Pro Pro Gly Pro Met Gly Pro Pro Gly Leu Pro Gly Leu Lys
1430 1435 1440

Gly Asp Pro Gly Ser Lys Gly Glu Lys Gly His Pro Gly Leu Ile
1445 1450 1455

Gly Leu Ile Gly Pro Pro Gly Glu Gln Gly Glu Lys Gly Asp Arg
1460 1465 1470

Gly Leu Pro Gly Thr Gln Gly Ser Pro Gly Ala Lys Gly Asp Gly
1475 1480 1485

Gly Ile Pro Gly Pro Ala Gly Pro Leu Gly Pro Pro Gly Pro Pro
1490 1495 1500

Gly Leu Pro Gly Pro Gln Gly Pro Lys Gly Asn Lys Gly Ser Thr
1505 1510 1515

Gly Pro Ala Gly Gln Lys Gly Asp Ser Gly Leu Pro Gly Pro Pro
1520 1525 1530

Gly Pro Pro Gly Pro Pro Gly Glu Val Ile Gln Pro Leu Pro Ile
1535 1540 1545

Leu Ser Ser Lys Lys Thr Arg Arg His Thr Glu Gly Met Gln Ala

1550 1555 1560

Asp Ala Asp Asp Asn Ile Leu Asp Tyr Ser Asp Gly Met Glu Glu
1565 1570 1575

Ile Phe Gly Ser Leu Asn Ser Leu Lys Gln Asp Ile Glu His Met
1580 1585 1590

Lys Phe Pro Met Gly Thr Gln Thr Asn Pro Ala Arg Thr Cys Lys
1595 1600 1605

Asp Leu Gln Leu Ser His Pro Asp Phe Pro Asp Gly Glu Tyr Trp
1610 1615 1620

Ile Asp Pro Asn Gln Gly Cys Ser Gly Asp Ser Phe Lys Val Tyr
1625 1630 1635

Cys Asn Phe Thr Ser Gly Gly Glu Thr Cys Ile Tyr Pro Asp Lys
1640 1645 1650

Lys Ser Glu Gly Val Arg Ile Ser Ser Trp Pro Lys Glu Lys Pro
1655 1660 1665

Gly Ser Trp Phe Ser Glu Phe Lys Arg Gly Lys Leu Leu Ser Tyr
1670 1675 1680

Leu Asp Val Glu Gly Asn Ser Ile Asn Met Val Gln Met Thr Phe
1685 1690 1695

Leu Lys Leu Leu Thr Ala Ser Ala Arg Gln Asn Phe Thr Tyr His
1700 1705 1710

Cys His Gln Ser Ala Ala Trp Tyr Asp Val Ser Ser Gly Ser Tyr
1715 1720 1725

Asp Lys Ala Leu Arg Phe Leu Gly Ser Asn Asp Glu Glu Met Ser
1730 1735 1740

Tyr Asp Asn Asn Pro Phe Ile Lys Thr Leu Tyr Asp Gly Cys Thr
1745 1750 1755

Ser Arg Lys Gly Tyr Glu Lys Thr Val Ile Glu Ile Asn Thr Pro
1760 1765 1770

Lys Ile Asp Gln Val Pro Ile Val Asp Val Met Ile Ser Asp Phe
1775 1780 1785

Gly Asp Gln Asn Gln Lys Phe Gly Phe Glu Val Gly Pro Val Cys
1790 1795 1800

Phe Leu Gly
1805

<210> 57
<211> 755
<212> PRT
<213> Homo sapiens

<400> 57

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Cys Lys Ala Ala Lys Ala Asp Leu Val Phe Met Val Asp Gly Ser Trp
1               5                  10                  15

Ser Ile Gly Asp Glu Asn Phe Asn Lys Ile Ile Ser Phe Leu Tyr Ser
            20                  25                  30

Thr Val Gly Ala Leu Asn Lys Ile Gly Thr Asp Gly Thr Gln Val Ala
        35                  40                  45

Met Val Gln Phe Thr Asp Asp Pro Arg Thr Glu Phe Lys Leu Asn Ala
    50                  55                  60

Tyr Lys Thr Lys Glu Thr Leu Leu Asp Ala Ile Lys His Ile Ser Tyr
65                  70                  75                  80

Lys Gly Gly Asn Thr Lys Thr Gly Lys Ala Ile Lys Tyr Val Arg Asp
                85                  90                  95

Thr Leu Phe Thr Ala Glu Ser Gly Thr Arg Arg Gly Ile Pro Lys Val
            100                 105                 110

Ile Val Val Ile Thr Asp Gly Arg Ser Gln Asp Asp Val Asn Lys Ile
        115                 120                 125

Ser Arg Glu Met Gln Leu Asp Gly Tyr Ser Ile Phe Ala Ile Gly Val
    130                 135                 140

Ala Asp Ala Asp Tyr Ser Glu Leu Val Ser Ile Gly Ser Lys Pro Ser
145                 150                 155                 160

Ala Arg His Val Phe Phe Val Asp Asp Phe Asp Ala Phe Lys Lys Ile
                165                 170                 175

Glu Asp Glu Leu Ile Thr Phe Val Cys Glu Thr Ala Ser Ala Thr Cys
            180                 185                 190

Pro Val Val His Lys Asp Gly Ile Asp Leu Ala Gly Phe Lys Met Met
        195                 200                 205

Glu Met Phe Gly Leu Val Glu Lys Asp Phe Ser Ser Val Glu Gly Val
    210                 215                 220

Ser Met Glu Pro Gly Thr Phe Asn Val Phe Pro Cys Tyr Gln Leu His
225                 230                 235                 240

Lys Asp Ala Leu Val Ser Gln Pro Thr Arg Tyr Leu His Pro Glu Gly
                245                 250                 255

Leu Pro Ser Asp Tyr Thr Ile Ser Phe Leu Phe Arg Ile Leu Pro Asp
            260                 265                 270

Thr Pro Gln Glu Pro Phe Ala Leu Trp Glu Ile Leu Asn Lys Asn Ser
        275                 280                 285

Asp Pro Leu Val Gly Val Ile Leu Asp Asn Gly Gly Lys Thr Leu Thr
    290                 295                 300

Tyr Phe Asn Tyr Asp Gln Ser Gly Asp Phe Gln Thr Val Thr Phe Glu
305                 310                 315                 320
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Gly Pro Glu Ile Arg Lys Ile Phe Tyr Gly Ser Phe His Lys Leu His
325 330 335

Ile Val Val Ser Glu Thr Leu Val Lys Val Val Ile Asp Cys Lys Gln
340 345 350

Val Gly Glu Lys Ala Met Asn Ala Ser Ala Asn Ile Thr Ser Asp Gly
355 360 365

Val Glu Val Leu Gly Lys Met Val Arg Ser Arg Gly Pro Gly Gly Asn
370 375 380

Ser Ala Pro Phe Gln Leu Gln Met Phe Asp Ile Val Cys Ser Thr Ser
385 390 395 400

Trp Ala Asn Thr Asp Lys Cys Cys Glu Leu Pro Gly Leu Arg Asp Asp
405 410 415

Glu Ser Cys Pro Asp Leu Pro His Ser Cys Ser Cys Ser Glu Thr Asn
420 425 430

Glu Val Ala Leu Gly Pro Ala Gly Pro Pro Gly Gly Pro Gly Leu Arg
435 440 445

Gly Pro Lys Gly Gln Gln Gly Glu Pro Gly Pro Lys Gly Pro Asp Gly
450 455 460

Pro Arg Gly Glu Ile Gly Leu Pro Gly Pro Gln Gly Pro Pro Gly Pro
465 470 475 480

Gln Gly Pro Ser Gly Leu Ser Ile Gln Gly Met Pro Gly Met Pro Gly
485 490 495

Glu Lys Gly Glu Lys Gly Asp Thr Gly Leu Pro Gly Pro Gln Gly Ile
500 505 510

Pro Gly Gly Val Gly Ser Pro Gly Arg Asp Gly Ser Pro Gly Gln Arg
515 520 525

Gly Leu Pro Gly Lys Asp Gly Ser Ser Gly Pro Pro Gly Pro Pro Gly
530 535 540

Pro Ile Gly Ile Pro Gly Thr Pro Gly Val Pro Gly Ile Thr Gly Ser
545 550 555 560

Met Gly Pro Gln Gly Ala Leu Gly Pro Pro Gly Val Pro Gly Ala Lys
565 570 575

Gly Glu Arg Gly Glu Arg Gly Asp Leu Gln Ser Gln Ala Met Val Arg
580 585 590

Ser Val Ala Arg Gln Val Cys Glu Gln Leu Ile Gln Ser His Met Ala
595 600 605

Arg Tyr Thr Ala Ile Leu Asn Gln Ile Pro Ser His Ser Ser Ser Ile
610 615 620

Arg Thr Val Gln Gly Pro Pro Gly Glu Pro Gly Arg Pro Gly Ser Pro
625 630 635 640

Gly Ala Pro Gly Glu Gln Gly Pro Pro Gly Thr Pro Gly Phe Pro Gly
645 650 655

Asn Ala Gly Val Pro Gly Thr Pro Gly Glu Arg Gly Leu Thr Gly Ile
660 665 670

Lys Gly Glu Lys Gly Asn Pro Gly Val Gly Thr Gln Gly Pro Arg Gly
675 680 685

Pro Pro Gly Pro Ala Gly Pro Ser Gly Glu Ser Arg Pro Gly Ser Pro
690 695 700

Gly Pro Pro Gly Ser Pro Gly Pro Arg Gly Pro Pro Gly His Leu Gly
705 710 715 720

Val Pro Gly Pro Gln Gly Pro Ser Gly Gln Pro Gly Tyr Cys Asp Pro
725 730 735

Ser Ser Cys Ser Ala Tyr Gly Val Arg Asp Leu Ile Pro Tyr Asn Asp
740 745 750

Tyr Gln His
755

<210> 58
<211> 543
<212> PRT
<213> Homo sapiens

<400> 58

Met Gly Thr Ser Leu Ser Pro Asn Asp Pro Trp Pro Leu Asn Pro Leu
1 5 10 15

Ser Ile Gln Gln Thr Thr Leu Leu Leu Leu Leu Ser Val Leu Ala Thr
20 25 30

Val His Val Gly Gln Arg Leu Leu Arg Gln Arg Arg Arg Gln Leu Arg
35 40 45

Ser Ala Pro Pro Gly Pro Phe Ala Trp Pro Leu Ile Gly Asn Ala Ala
50 55 60

Ala Val Gly Gln Ala Ala His Leu Ser Phe Ala Arg Leu Ala Arg Arg
65 70 75 80

Tyr Gly Asp Val Phe Gln Ile Arg Leu Gly Ser Cys Pro Ile Val Val
85 90 95

Leu Asn Gly Glu Arg Ala Ile His Gln Ala Leu Val Gln Gln Gly Ser
100 105 110

Ala Phe Ala Asp Arg Pro Ala Phe Ala Ser Phe Arg Val Val Ser Gly
115 120 125

Gly Arg Ser Met Ala Phe Gly His Tyr Ser Glu His Trp Lys Val Gln
130 135 140

Arg Arg Ala Ala His Ser Met Met Arg Asn Phe Phe Thr Arg Gln Pro
145 150 155 160

Arg Ser Arg Gln Val Leu Glu Gly His Val Leu Ser Glu Ala Arg Glu
165 170 175

Leu Val Ala Leu Leu Val Arg Gly Ser Ala Asp Gly Ala Phe Leu Asp
180 185 190

Pro Arg Pro Leu Thr Val Val Ala Val Ala Asn Val Met Ser Ala Val
195 200 205

Cys Phe Gly Cys Arg Tyr Ser His Asp Asp Pro Glu Phe Arg Glu Leu
210 215 220

Leu Ser His Asn Glu Glu Phe Gly Arg Thr Val Gly Ala Gly Ser Leu
225 230 235 240

Val Asp Val Met Pro Trp Leu Gln Tyr Phe Pro Asn Pro Val Arg Thr
245 250 255

Val Phe Arg Glu Phe Glu Gln Leu Asn Arg Asn Phe Ser Asn Phe Ile
260 265 270

Leu Asp Lys Phe Leu Arg His Cys Glu Ser Leu Arg Pro Gly Ala Ala
275 280 285

Pro Arg Asp Met Met Asp Ala Phe Ile Leu Ser Ala Glu Lys Lys Ala
290 295 300

Ala Gly Asp Ser His Gly Gly Gly Ala Arg Leu Asp Leu Glu Asn Val
305 310 315 320

Pro Ala Thr Ile Thr Asp Ile Phe Gly Ala Ser Gln Asp Thr Leu Ser
325 330 335

Thr Ala Leu Gln Trp Leu Leu Leu Leu Phe Thr Arg Tyr Pro Asp Val
340 345 350

Gln Thr Arg Val Gln Ala Glu Leu Asp Gln Val Val Gly Arg Asp Arg
355 360 365

Leu Pro Cys Met Gly Asp Gln Pro Asn Leu Pro Tyr Val Leu Ala Phe
370 375 380

Leu Tyr Glu Ala Met Arg Phe Ser Ser Phe Val Pro Val Thr Ile Pro
385 390 395 400

His Ala Thr Thr Ala Asn Thr Ser Val Leu Gly Tyr His Ile Pro Lys
405 410 415

Asp Thr Val Val Phe Val Asn Gln Trp Ser Val Asn His Asp Pro Val
420 425 430

Lys Trp Pro Asn Pro Glu Asn Phe Asp Pro Ala Arg Phe Leu Asp Lys
435 440 445

Asp Gly Leu Ile Asn Lys Asp Leu Thr Ser Arg Val Met Ile Phe Ser
450 455 460

Val Gly Lys Arg Arg Cys Ile Gly Glu Glu Leu Ser Lys Met Gln Leu
465 470 475 480

Phe Leu Phe Ile Ser Ile Leu Ala His Gln Cys Asp Phe Arg Ala Asn
485 490 495

Pro Asn Glu Pro Ala Lys Met Asn Phe Ser Tyr Gly Leu Thr Ile Lys
500 505 510

Pro Lys Ser Phe Lys Val Asn Val Thr Leu Arg Glu Ser Met Glu Leu
515 520 525

Leu Asp Ser Ala Val Gln Asn Leu Gln Ala Lys Glu Thr Cys Gln
530 535 540

<210> 59
<211> 767
<212> PRT
<213> Homo sapiens

<400> 59

Met Ser Gln Arg Pro Arg Ala Pro Arg Ser Ala Leu Trp Leu Leu Ala
1 5 10 15

Pro Pro Leu Leu Arg Trp Ala Pro Pro Leu Leu Thr Val Leu His Ser
20 25 30

Asp Leu Phe Gln Ala Leu Leu Asp Ile Leu Asp Tyr Tyr Glu Ala Ser
35 40 45

Leu Ser Glu Ser Gln Lys Tyr Arg Tyr Gln Asp Glu Asp Thr Pro Pro
50 55 60

Leu Glu His Ser Pro Ala His Leu Pro Asn Gln Ala Asn Ser Pro Pro
65 70 75 80

Val Ile Val Asn Thr Asp Thr Leu Glu Ala Pro Gly Tyr Glu Leu Gln
85 90 95

Val Asn Gly Thr Glu Gly Glu Met Glu Tyr Glu Glu Ile Thr Leu Glu
100 105 110

Arg Gly Asn Ser Gly Leu Gly Phe Ser Ile Ala Gly Gly Thr Asp Asn
115 120 125

Pro His Ile Gly Asp Asp Pro Ser Ile Phe Ile Thr Lys Ile Ile Pro
130 135 140

Gly Gly Ala Ala Ala Gln Asp Gly Arg Leu Arg Val Asn Asp Ser Ile
145 150 155 160

Leu Phe Val Asn Glu Val Asp Val Arg Glu Val Thr His Ser Ala Ala
165 170 175

Val Glu Ala Leu Lys Glu Ala Gly Ser Ile Val Arg Leu Tyr Val Met
180 185 190

Arg Arg Lys Pro Pro Ala Glu Lys Val Met Glu Ile Lys Leu Ile Lys
195 200 205

Gly Pro Lys Gly Leu Gly Phe Ser Ile Ala Gly Gly Val Gly Asn Gln

210 215 220

His Ile Pro Gly Asp Asn Ser Ile Tyr Val Thr Lys Ile Ile Glu Gly
225 230 235 240

Gly Ala Ala His Lys Asp Gly Arg Leu Gln Ile Gly Asp Lys Ile Leu
245 250 255

Ala Val Asn Ser Val Gly Leu Glu Asp Val Met His Glu Asp Ala Val
260 265 270

Ala Ala Leu Lys Asn Thr Tyr Asp Val Val Tyr Leu Lys Val Ala Lys
275 280 285

Pro Ser Asn Ala Tyr Leu Ser Asp Ser Tyr Ala Pro Pro Asp Ile Thr
290 295 300

Thr Ser Tyr Ser Gln His Leu Asp Asn Glu Ile Ser His Ser Ser Tyr
305 310 315 320

Leu Gly Thr Asp Tyr Pro Thr Ala Met Thr Pro Thr Ser Pro Arg Arg
325 330 335

Tyr Ser Pro Val Ala Lys Asp Leu Leu Gly Glu Glu Asp Ile Pro Arg
340 345 350

Glu Pro Arg Arg Ile Val Ile His Arg Gly Ser Thr Gly Leu Gly Phe
355 360 365

Asn Ile Val Gly Gly Glu Asp Gly Glu Gly Ile Phe Ile Ser Phe Ile
370 375 380

Leu Ala Gly Gly Pro Ala Asp Leu Ser Gly Glu Leu Arg Lys Gly Asp
385 390 395 400

Gln Ile Leu Ser Val Asn Gly Val Asp Leu Arg Asn Ala Ser His Glu
405 410 415

Gln Ala Ala Ile Ala Leu Lys Asn Ala Gly Gln Thr Val Thr Ile Ile
420 425 430

Ala Gln Tyr Lys Pro Glu Glu Tyr Ser Arg Phe Glu Ala Lys Ile His
435 440 445

Asp Leu Arg Glu Gln Leu Met Asn Ser Ser Leu Gly Ser Gly Thr Ala
450 455 460

Ser Leu Arg Ser Asn Pro Lys Arg Gly Phe Tyr Ile Arg Ala Leu Phe
465 470 475 480

Asp Tyr Asp Lys Thr Lys Asp Cys Gly Phe Leu Ser Gln Ala Leu Ser
485 490 495

Phe Arg Phe Gly Asp Val Leu His Val Ile Asp Ala Ser Asp Glu Glu
500 505 510

Trp Trp Gln Ala Arg Arg Val His Ser Asp Ser Glu Thr Asp Asp Ile
515 520 525

Gly Phe Ile Pro Ser Lys Arg Arg Val Glu Arg Arg Glu Trp Ser Arg

530 535 540

Leu Lys Ala Lys Asp Trp Gly Ser Ser Ser Gly Ser Gln Gly Arg Glu
545 550 555 560

Asp Ser Val Leu Ser Tyr Glu Thr Val Thr Gln Met Glu Val His Tyr
565 570 575

Ala Arg Pro Ile Ile Ile Leu Gly Pro Thr Lys Asp Arg Ala Asn Asp
580 585 590

Asp Leu Leu Ser Glu Phe Pro Asp Lys Phe Gly Ser Cys Val Pro His
595 600 605

Thr Thr Arg Pro Lys Arg Glu Tyr Glu Ile Asp Gly Arg Asp Tyr His
610 615 620

Phe Val Ser Ser Arg Glu Lys Met Glu Lys Asp Ile Gln Ala His Lys
625 630 635 640

Phe Ile Glu Ala Gly Gln Tyr Asn Ser His Leu Tyr Gly Thr Ser Val
645 650 655

Gln Ser Val Arg Glu Val Ala Glu Gln Gly Lys His Cys Ile Leu Asp
660 665 670

Val Ser Ala Asn Ala Val Arg Arg Leu Gln Ala Ala His Leu His Pro
675 680 685

Ile Ala Ile Phe Ile Arg Pro Arg Ser Leu Glu Asn Val Leu Glu Ile
690 695 700

Asn Lys Arg Ile Thr Glu Glu Gln Ala Arg Lys Ala Phe Asp Arg Ala
705 710 715 720

Thr Lys Leu Glu Gln Glu Phe Thr Glu Cys Phe Ser Ala Ile Val Glu
725 730 735

Gly Asp Ser Phe Glu Glu Ile Tyr His Lys Val Lys Arg Val Ile Glu
740 745 750

Asp Leu Ser Gly Pro Tyr Ile Trp Val Pro Ala Arg Glu Arg Leu
755 760 765

<210> 60
<211> 367
<212> PRT
<213> Homo sapiens

<400> 60

Met Val Met Glu Val Gly Thr Leu Asp Ala Gly Gly Leu Arg Ala Leu
1 5 10 15

Leu Gly Glu Arg Ala Ala Gln Cys Leu Leu Leu Asp Cys Arg Ser Phe
20 25 30

Phe Ala Phe Asn Ala Gly His Ile Ala Gly Ser Val Asn Val Arg Phe
35 40 45

Ser Thr Ile Val Arg Arg Arg Ala Lys Gly Ala Met Gly Leu Glu His
50 55 60

Ile Val Pro Asn Ala Glu Leu Arg Gly Arg Leu Leu Ala Gly Ala Tyr
65 70 75 80

His Ala Val Val Leu Leu Asp Glu Arg Ser Ala Ala Leu Asp Gly Ala
85 90 95

Lys Arg Asp Gly Thr Leu Ala Leu Ala Ala Gly Ala Leu Cys Arg Glu
100 105 110

Ala Arg Ala Ala Gln Val Phe Phe Leu Lys Gly Gly Tyr Glu Ala Phe
115 120 125

Ser Ala Ser Cys Pro Glu Leu Cys Ser Lys Gln Ser Thr Pro Met Gly
130 135 140

Leu Ser Leu Pro Leu Ser Thr Ser Val Pro Asp Ser Ala Glu Ser Gly
145 150 155 160

Cys Ser Ser Cys Ser Thr Pro Leu Tyr Asp Gln Gly Gly Pro Val Glu
165 170 175

Ile Leu Pro Phe Leu Tyr Leu Gly Ser Ala Tyr His Ala Ser Arg Lys
180 185 190

Asp Met Leu Asp Ala Leu Gly Ile Thr Ala Leu Ile Asn Val Ser Ala
195 200 205

Asn Cys Pro Asn His Phe Glu Gly His Tyr Gln Tyr Lys Ser Ile Pro
210 215 220

Val Glu Asp Asn His Lys Ala Asp Ile Ser Ser Trp Phe Asn Glu Ala
225 230 235 240

Ile Asp Phe Ile Asp Ser Ile Lys Asn Ala Gly Gly Arg Val Phe Val
245 250 255

His Cys Gln Ala Gly Ile Ser Arg Ser Ala Thr Ile Cys Leu Ala Tyr
260 265 270

Leu Met Arg Thr Asn Arg Val Lys Leu Asp Glu Ala Phe Glu Phe Val
275 280 285

Lys Gln Arg Arg Ser Ile Ile Ser Pro Asn Phe Ser Phe Met Gly Gln
290 295 300

Leu Leu Gln Phe Glu Ser Gln Val Leu Ala Pro His Cys Ser Ala Glu
305 310 315 320

Ala Gly Ser Pro Ala Met Ala Val Leu Asp Arg Gly Thr Ser Thr Thr
325 330 335

Thr Val Phe Asn Phe Pro Val Ser Ile Pro Val His Ser Thr Asn Ser
340 345 350

Ala Leu Ser Tyr Leu Gln Ser Pro Ile Thr Thr Ser Pro Ser Cys
355 360 365

<210> 61
<211> 345
<212> PRT
<213> Homo sapiens

<400> 61

Met Ala Ala Ala Glu Pro Ala Ser Ser Gly Gln Gln Ala Pro Ala Gly
1 5 10 15

Gln Gly Gln Gly Gln Arg Pro Pro Pro Gln Pro Pro Gln Ala Gln Ala
20 25 30

Pro Gln Pro Pro Pro Pro Pro Gln Leu Gly Gly Ala Gly Gly Gly Ser
35 40 45

Ser Arg His Glu Lys Ser Leu Gly Leu Leu Thr Thr Lys Phe Val Ser
50 55 60

Leu Leu Gln Glu Ala Lys Asp Gly Val Leu Asp Leu Lys Ala Ala Ala
65 70 75 80

Asp Thr Leu Ala Val Arg Gln Lys Arg Arg Ile Tyr Asp Ile Thr Asn
85 90 95

Val Leu Glu Gly Ile Asp Leu Ile Glu Lys Lys Ser Lys Asn Ser Ile
100 105 110

Gln Trp Lys Gly Val Gly Ala Gly Cys Asn Thr Lys Glu Val Ile Asp
115 120 125

Arg Leu Arg Tyr Leu Lys Ala Glu Ile Glu Asp Leu Glu Leu Lys Glu
130 135 140

Arg Glu Leu Asp Gln Gln Lys Leu Trp Leu Gln Gln Ser Ile Lys Asn
145 150 155 160

Val Met Asp Asp Ser Ile Asn Asn Arg Phe Ser Tyr Val Thr His Glu
165 170 175

Asp Ile Cys Asn Cys Phe Asn Gly Asp Thr Leu Leu Ala Ile Gln Ala
180 185 190

Pro Ser Gly Thr Gln Leu Glu Val Pro Ile Pro Glu Met Gly Gln Asn
195 200 205

Gly Gln Lys Lys Tyr Gln Ile Asn Leu Lys Ser His Ser Gly Pro Ile
210 215 220

His Val Leu Leu Ile Asn Lys Glu Ser Ser Ser Ser Lys Pro Val Val
225 230 235 240

Phe Pro Val Pro Pro Pro Asp Asp Leu Thr Gln Pro Ser Ser Gln Ser
245 250 255

Leu Thr Pro Val Thr Pro Gln Lys Ser Ser Met Ala Thr Gln Asn Leu
260 265 270

Pro Glu Gln His Val Ser Glu Arg Ser Gln Ala Leu Gln Gln Thr Ser
275 280 285

Ala Thr Asp Ile Ser Ser Gly Ser Ile Ser Gly Asp Ile Ile Asp Glu
290 295 300

Leu Met Ser Ser Asp Val Phe Pro Leu Leu Arg Leu Ser Pro Thr Pro
305 310 315 320

Ala Asp Asp Tyr Asn Phe Asn Leu Asp Asp Asn Glu Gly Val Cys Asp
325 330 335

Leu Phe Asp Val Gln Ile Leu Asn Tyr
340 345

<210> 62
<211> 427
<212> PRT
<213> Homo sapiens

<400> 62

Met Glu Thr Leu Cys Leu Arg Ala Ser Phe Trp Leu Ala Leu Val Gly
1 5 10 15

Cys Val Ile Ser Asp Asn Pro Glu Arg Tyr Ser Thr Asn Leu Ser Asn
20 25 30

His Val Asp Asp Phe Thr Thr Phe Arg Gly Thr Glu Leu Ser Phe Leu
35 40 45

Val Thr Thr His Gln Pro Thr Asn Leu Val Leu Pro Ser Asn Gly Ser
50 55 60

Met His Asn Tyr Cys Pro Gln Gln Thr Lys Ile Thr Ser Ala Phe Lys
65 70 75 80

Tyr Ile Asn Thr Val Ile Ser Cys Thr Ile Phe Ile Val Gly Met Val
85 90 95

Gly Asn Ala Thr Leu Leu Arg Ile Ile Tyr Gln Asn Lys Cys Met Arg
100 105 110

Asn Gly Pro Asn Ala Leu Ile Ala Ser Leu Ala Leu Gly Asp Leu Ile
115 120 125

Tyr Val Val Ile Asp Leu Pro Ile Asn Val Phe Lys Leu Leu Ala Gly
130 135 140

Arg Trp Pro Phe Asp His Asn Asp Phe Gly Val Phe Leu Cys Lys Leu
145 150 155 160

Phe Pro Phe Leu Gln Lys Ser Ser Val Gly Ile Thr Val Leu Asn Leu
165 170 175

Cys Ala Leu Ser Val Asp Arg Tyr Arg Ala Val Ala Ser Trp Ser Arg
180 185 190

Val Gln Gly Ile Gly Ile Pro Leu Val Thr Ala Ile Glu Ile Val Ser
195 200 205

Ile Trp Ile Leu Ser Phe Ile Leu Ala Ile Pro Glu Ala Ile Gly Phe

210 215 220

Val Met Val Pro Phe Glu Tyr Arg Gly Glu Gln His Lys Thr Cys Met
225 230 235 240

Leu Asn Ala Thr Ser Lys Phe Met Glu Phe Tyr Gln Asp Val Lys Asp
245 250 255

Trp Trp Leu Phe Gly Phe Tyr Phe Cys Met Pro Leu Val Cys Thr Ala
260 265 270

Ile Phe Tyr Thr Leu Met Thr Cys Glu Met Leu Asn Arg Arg Asn Gly
275 280 285

Ser Leu Arg Ile Ala Leu Ser Glu His Leu Lys Gln Arg Arg Glu Val
290 295 300

Ala Lys Thr Val Phe Cys Leu Val Val Ile Phe Ala Leu Cys Trp Phe
305 310 315 320

Pro Leu His Leu Ser Arg Ile Leu Lys Lys Thr Val Tyr Asn Glu Met
325 330 335

Asp Lys Asn Arg Cys Glu Leu Leu Ser Phe Leu Leu Leu Met Asp Tyr
340 345 350

Ile Gly Ile Asn Leu Ala Thr Met Asn Ser Cys Ile Asn Pro Ile Ala
355 360 365

Leu Tyr Phe Val Ser Lys Lys Phe Lys Asn Cys Phe Gln Ser Cys Leu
370 375 380

Cys Cys Cys Cys Tyr Gln Ser Lys Ser Leu Met Thr Ser Val Pro Met
385 390 395 400

Asn Gly Thr Ser Ile Gln Trp Lys Asn His Asp Gln Asn Asn His Asn
405 410 415

Thr Asp Arg Ser Ser His Lys Asp Ser Met Asn
420 425

<210> 63
<211> 405
<212> PRT
<213> Homo sapiens

<400> 63

Met Glu Arg Leu Gln Lys Gln Pro Leu Thr Ser Pro Gly Ser Val Ser
1 5 10 15

Pro Ser Arg Asp Ser Ser Val Pro Gly Ser Pro Ser Ser Ile Val Ala
20 25 30

Lys Met Asp Asn Gln Val Leu Gly Tyr Lys Asp Leu Ala Ala Ile Pro
35 40 45

Lys Asp Lys Ala Ile Leu Asp Ile Glu Arg Pro Asp Leu Met Ile Tyr
50 55 60

Glu Pro His Phe Thr Tyr Ser Leu Leu Glu His Val Glu Leu Pro Arg
65 70 75 80

Gln Arg Glu Arg Ser Leu Ser Pro Lys Ser Thr Ser Pro Pro Pro Ser
85 90 95

Pro Glu Val Trp Ala Asp Ser Arg Ser Pro Gly Ile Ile Ser Gln Ala
100 105 110

Ser Ala Pro Arg Thr Thr Gly Thr Pro Arg Thr Ser Leu Pro His Phe
115 120 125

His His Pro Glu Thr Ser Arg Pro Asp Ser Asn Ile Tyr Lys Lys Pro
130 135 140

Pro Ile Tyr Lys Gln Arg Glu Ser Val Gly Gly Ser Pro Gln Thr Lys
145 150 155 160

His Leu Ile Glu Asp Leu Ile Ile Glu Ser Ser Lys Phe Pro Ala Ala
165 170 175

Gln Pro Pro Asp Pro Asn Gln Pro Ala Lys Ile Glu Thr Asp Tyr Trp
180 185 190

Pro Cys Pro Pro Ser Leu Ala Val Val Glu Thr Glu Trp Arg Lys Arg
195 200 205

Lys Ala Ser Arg Arg Gly Ala Glu Glu Glu Glu Glu Glu Glu Asp Asp
210 215 220

Asp Ser Gly Glu Glu Met Lys Ala Leu Arg Glu Arg Gln Arg Glu Glu
225 230 235 240

Leu Ser Lys Val Thr Ser Asn Leu Gly Lys Met Ile Leu Lys Glu Glu
245 250 255

Met Glu Lys Ser Leu Pro Ile Arg Arg Lys Thr Arg Ser Leu Pro Asp
260 265 270

Arg Thr Pro Phe His Thr Ser Leu His Gln Gly Thr Ser Lys Ser Ser
275 280 285

Ser Leu Pro Arg Tyr Gly Arg Thr Thr Leu Ser Arg Leu Gln Ser Thr
290 295 300

Glu Phe Ser Pro Ser Gly Ser Glu Thr Gly Ser Pro Gly Leu Gln Asn
305 310 315 320

Gly Glu Gly Gln Arg Gly Arg Met Asp Arg Gly Asn Ser Leu Pro Cys
325 330 335

Val Leu Glu Gln Lys Ile Tyr Pro Tyr Glu Met Leu Val Val Thr Asn
340 345 350

Lys Gly Arg Thr Lys Leu Pro Pro Gly Val Asp Arg Met Arg Leu Glu
355 360 365

Arg His Leu Ser Ala Glu Asp Phe Ser Arg Val Phe Ala Met Ser Pro
370 375 380

Glu Glu Phe Gly Lys Leu Ala Leu Trp Lys Arg Asn Glu Leu Lys Lys
385 390 395 400

Lys Ala Ser Leu Phe
405

<210> 64
<211> 916
<212> PRT
<213> Homo sapiens

<400> 64

Met Glu Ser Gly Gln Pro Ala Arg Arg Ile Ala Met Ala Pro Leu Leu
1 5 10 15

Glu Tyr Glu Arg Gln Leu Val Leu Glu Leu Leu Asp Thr Asp Gly Leu
20 25 30

Val Val Cys Ala Arg Gly Leu Gly Ala Asp Arg Leu Leu Tyr His Phe
35 40 45

Leu Gln Leu His Cys His Pro Ala Cys Leu Val Leu Val Leu Asn Thr
50 55 60

Gln Pro Ala Glu Glu Glu Tyr Phe Ile Asn Gln Leu Lys Ile Glu Gly
65 70 75 80

Val Glu His Leu Pro Arg Arg Val Thr Asn Glu Ile Thr Ser Asn Ser
85 90 95

Arg Tyr Glu Val Tyr Thr Gln Gly Gly Val Ile Phe Ala Thr Ser Arg
100 105 110

Ile Leu Val Val Asp Phe Leu Thr Asp Arg Ile Pro Ser Asp Leu Ile
115 120 125

Thr Gly Ile Leu Val Tyr Arg Ala His Arg Ile Ile Glu Ser Cys Gln
130 135 140

Glu Ala Phe Ile Leu Arg Leu Phe Arg Gln Lys Asn Lys Arg Gly Phe
145 150 155 160

Ile Lys Ala Phe Thr Asp Asn Ala Val Ala Phe Asp Thr Gly Phe Cys
165 170 175

His Val Glu Arg Val Met Arg Asn Leu Phe Val Arg Lys Leu Tyr Leu
180 185 190

Trp Pro Arg Phe His Val Ala Val Asn Ser Phe Leu Glu Gln His Lys
195 200 205

Pro Glu Val Val Glu Ile His Val Ser Met Thr Pro Thr Met Leu Ala
210 215 220

Ile Gln Thr Ala Ile Leu Asp Ile Leu Asn Ala Cys Leu Lys Glu Leu
225 230 235 240

Lys Cys His Asn Pro Ser Leu Glu Val Glu Asp Leu Ser Leu Glu Asn
245 250 255

Ala Ile Gly Lys Pro Phe Asp Lys Thr Ile Arg His Tyr Leu Asp Pro
260 265 270

Leu Trp His Gln Leu Gly Ala Lys Thr Lys Ser Leu Val Gln Asp Leu
275 280 285

Lys Ile Leu Arg Thr Leu Leu Gln Tyr Leu Ser Gln Tyr Asp Cys Val
290 295 300

Thr Phe Leu Asn Leu Leu Glu Ser Leu Arg Ala Thr Glu Lys Ala Phe
305 310 315 320

Gly Gln Asn Ser Gly Trp Leu Phe Leu Asp Ser Ser Thr Ser Met Phe
325 330 335

Ile Asn Ala Arg Ala Arg Val Tyr His Leu Pro Asp Ala Lys Met Ser
340 345 350

Lys Lys Glu Lys Ile Ser Glu Lys Met Glu Ile Lys Glu Gly Glu Glu
355 360 365

Thr Lys Lys Glu Leu Val Leu Glu Ser Asn Pro Lys Trp Glu Ala Leu
370 375 380

Thr Glu Val Leu Lys Glu Ile Glu Ala Glu Asn Lys Glu Ser Glu Ala
385 390 395 400

Leu Gly Gly Pro Gly Gln Val Leu Ile Cys Ala Ser Asp Asp Arg Thr
405 410 415

Cys Ser Gln Leu Arg Asp Tyr Ile Thr Leu Gly Ala Glu Ala Phe Leu
420 425 430

Leu Arg Leu Tyr Arg Lys Thr Phe Glu Lys Asp Ser Lys Ala Glu Glu
435 440 445

Val Trp Met Lys Phe Arg Lys Glu Asp Ser Ser Lys Arg Ile Arg Lys
450 455 460

Ser His Lys Arg Pro Lys Asp Pro Gln Asn Lys Glu Arg Ala Ser Thr
465 470 475 480

Lys Glu Arg Thr Leu Lys Lys Lys Lys Arg Lys Leu Thr Leu Thr Gln
485 490 495

Met Val Gly Lys Pro Glu Glu Leu Glu Glu Glu Gly Asp Val Glu Glu
500 505 510

Gly Tyr Arg Arg Glu Ile Ser Ser Ser Pro Glu Ser Cys Pro Glu Glu
515 520 525

Ile Lys His Glu Glu Phe Asp Val Asn Leu Ser Ser Asp Ala Ala Phe
530 535 540

Gly Ile Leu Lys Glu Pro Leu Thr Ile Ile His Pro Leu Leu Gly Cys
545 550 555 560

Ser Asp Pro Tyr Ala Leu Thr Arg Val Leu His Glu Val Glu Pro Arg
565 570 575

Tyr Val Val Leu Tyr Asp Ala Glu Leu Thr Phe Val Arg Gln Leu Glu
580 585 590

Ile Tyr Arg Ala Ser Arg Pro Gly Lys Pro Leu Arg Val Tyr Phe Leu
595 600 605

Ile Tyr Gly Gly Ser Thr Glu Glu Gln Arg Tyr Leu Thr Ala Leu Arg
610 615 620

Lys Glu Lys Glu Ala Phe Glu Lys Leu Ile Arg Glu Lys Ala Ser Met
625 630 635 640

Val Val Pro Glu Glu Arg Glu Gly Arg Asp Glu Thr Asn Leu Asp Leu
645 650 655

Val Arg Gly Thr Ala Ser Ala Asp Val Ser Thr Asp Thr Arg Lys Ala
660 665 670

Gly Gly Gln Glu Gln Asn Gly Thr Gln Gln Ser Ile Val Val Asp Met
675 680 685

Arg Glu Phe Arg Ser Glu Leu Pro Ser Leu Ile His Arg Arg Gly Ile
690 695 700

Asp Ile Glu Pro Val Thr Leu Glu Val Gly Asp Tyr Ile Leu Thr Pro
705 710 715 720

Glu Met Cys Val Glu Arg Lys Ser Ile Ser Asp Leu Ile Gly Ser Leu
725 730 735

Asn Asn Gly Arg Leu Tyr Ser Gln Cys Ile Ser Met Ser Arg Tyr Tyr
740 745 750

Lys Arg Pro Val Leu Leu Ile Glu Phe Asp Pro Ser Lys Pro Phe Ser
755 760 765

Leu Thr Ser Arg Gly Ala Leu Phe Gln Glu Ile Ser Ser Asn Asp Ile
770 775 780

Ser Ser Lys Leu Thr Leu Leu Thr Leu His Phe Pro Arg Leu Arg Ile
785 790 795 800

Leu Trp Cys Pro Ser Pro His Ala Thr Ala Glu Leu Phe Glu Glu Leu
805 810 815

Lys Gln Ser Lys Pro Gln Pro Asp Ala Ala Thr Ala Leu Ala Ile Thr
820 825 830

Ala Asp Ser Glu Thr Leu Pro Glu Ser Glu Lys Tyr Asn Pro Gly Pro
835 840 845

Gln Asp Phe Leu Leu Lys Met Pro Gly Val Asn Ala Lys Asn Cys Arg
850 855 860

Ser Leu Met His His Val Lys Asn Ile Ala Glu Leu Ala Ala Leu Ser
865 870 875 880

Gln Asp Glu Leu Thr Ser Ile Leu Gly Asn Ala Ala Asn Ala Lys Gln
885 890 895

Leu Tyr Asp Phe Ile His Thr Ser Phe Ala Glu Val Val Ser Lys Gly
900 905 910

Lys Gly Lys Lys
915

<210> 65
<211> 297
<212> PRT
<213> Homo sapiens

<400> 65

Glu Phe Gly Ala Lys Ser Asn Gln Gln Leu Asp Arg Lys Arg Met Ala
1 5 10 15

Leu Lys Gln Ile Ser Ser Asn Lys Cys Phe Gly Gly Leu Gln Lys Val
20 25 30

Phe Glu His Asp Ser Val Glu Leu Asn Cys Lys Met Lys Phe Ala Val
35 40 45

Tyr Leu Pro Pro Lys Ala Glu Thr Gly Lys Cys Pro Ala Cys Ile Gly
50 55 60

Ser Pro Gly Leu Thr Cys Thr Glu Pro Lys Phe Tyr His Gln Asn Leu
65 70 75 80

Val Ile Ile Ser Leu Leu Gln Asn His Leu Ser Cys Cys His Cys Ser
85 90 95

Arg Tyr Ser Pro Arg Ala Cys Asn Ile Lys Gly Glu Asp Glu Ser Trp
100 105 110

Asp Phe Ala Thr Gly Arg Gly Phe Tyr Val Asp Ala Thr Glu Asp Pro
115 120 125

Trp Lys Thr Asn Tyr Arg Met Tyr Ser Tyr Val Thr Glu Glu Leu Pro
130 135 140

Gln Leu Ile Asn Ala Asn Phe Pro Val Asp Pro Gln Arg Met Ser Ile
145 150 155 160

Phe Gly His Ser Met Gly Gly His Gly Ala Leu Ile Cys Ala Leu Lys
165 170 175

Asn Pro Gly Lys Tyr Lys Ser Val Ser Ala Phe Ala Pro Ile Cys Asn
180 185 190

Pro Val Leu Cys Pro Trp Gly Lys Lys Ala Phe Ser Gly Tyr Leu Gly
195 200 205

Thr Asp Gln Ser Lys Trp Lys Ala Tyr Asp Ala Thr His Leu Val Lys
210 215 220

Ser Tyr Pro Gly Ser Gln Leu Asp Ile Leu Ile Asp Gln Gly Lys Asp
225 230 235 240

Asp Gln Phe Leu Leu Asp Gly Gln Leu Leu Pro Asp Asn Phe Ile Ala

245 250 255

Ala Cys Thr Glu Lys Lys Ile Pro Val Val Phe Arg Leu Gln Glu Gly
260 265 270

Tyr Asp His Ser Tyr Tyr Phe Ile Ala Thr Phe Ile Thr Asp His Ile
275 280 285

Arg His His Ala Lys Tyr Leu Asn Ala
290 295

<210> 66
<211> 756
<212> PRT
<213> Homo sapiens

<400> 66

Met Ser Pro Gln Lys Arg Val Lys Asn Val Gln Ala Gln Asn Arg Thr
1 5 10 15

Ser Gln Gly Ser Ser Ser Phe Gln Thr Thr Leu Ser Ala Trp Lys Val
20 25 30

Lys Gln Asp Pro Ser Asn Ser Lys Asn Ile Ser Lys His Gly Gln Asn
35 40 45

Asn Pro Val Gly Asp Tyr Glu His Ala Asp Asp Gln Ala Glu Glu Asp
50 55 60

Ala Leu Gln Met Ala Val Gly Tyr Phe Glu Lys Gly Pro Ile Lys Ala
65 70 75 80

Ser Gln Asn Lys Asp Lys Thr Leu Glu Lys His Leu Lys Thr Val Glu
85 90 95

Asn Val Ala Trp Lys Asn Gly Leu Ala Ser Glu Glu Ile Asp Ile Leu
100 105 110

Leu Asn Ile Ala Leu Ser Gly Lys Phe Gly Asn Ala Val Asn Thr Arg
115 120 125

Ile Leu Lys Cys Met Ile Pro Ala Thr Val Ile Ser Glu Asp Ser Val
130 135 140

Val Lys Ala Val Ser Trp Leu Cys Val Gly Lys Cys Ser Gly Ser Thr
145 150 155 160

Lys Val Leu Phe Tyr Arg Trp Leu Val Ala Met Phe Asp Phe Ile Asp
165 170 175

Arg Lys Glu Gln Ile Asn Leu Leu Tyr Gly Phe Phe Phe Ala Ser Leu
180 185 190

Gln Asp Asp Ala Leu Cys Pro Tyr Val Cys His Leu Leu Tyr Leu Leu
195 200 205

Thr Lys Lys Glu Asn Val Lys Pro Phe Arg Val Arg Lys Leu Leu Asp
210 215 220

Leu Gln Ala Lys Met Gly Met Gln Pro His Leu Gln Ala Leu Leu Ser
225 230 235 240

Leu Tyr Lys Phe Phe Ala Pro Ala Leu Ile Ser Val Ser Leu Pro Val
245 250 255

Arg Lys Lys Ile Tyr Leu Gln Asn Ser Glu Asn Leu Trp Lys Thr Ala
260 265 270

Leu Leu Ala Val Lys Gln Arg Asn Arg Gly Pro Ser Pro Glu Pro Leu
275 280 285

Lys Leu Met Leu Gly Pro Ala Asn Val Arg Pro Leu Lys Arg Lys Trp
290 295 300

Asn Ser Leu Ser Val Ile Pro Val Leu Asn Ser Ser Ser Tyr Thr Lys
305 310 315 320

Glu Cys Gly Lys Lys Glu Met Ser Leu Ser Asp Cys Leu Asn Arg Ser
325 330 335

Gly Ser Phe Pro Leu Glu Gln Leu Gln Ser Phe Pro Gln Leu Leu Gln
340 345 350

Asn Ile His Cys Leu Glu Leu Pro Ser Gln Met Gly Ser Val Leu Asn
355 360 365

Asn Ser Leu Leu Leu His Tyr Ile Asn Cys Val Arg Asp Glu Pro Val
370 375 380

Leu Leu Arg Phe His Tyr Trp Leu Ser Gln Thr Leu Gln Glu Glu Cys
385 390 395 400

Ile Trp Tyr Lys Val Asn Asn Tyr Glu His Gly Lys Glu Phe Thr Asn
405 410 415

Phe Leu Asp Thr Ile Ile Arg Ala Glu Cys Phe Leu Gln Glu Gly Tyr
420 425 430

Tyr Ser Cys Glu Ala Phe Leu Tyr Lys Ser Leu Pro Leu Trp Asp Gly
435 440 445

Leu Ser Cys Arg Ser Gln Phe Leu Gln Leu Val Ser Trp Ile Pro Phe
450 455 460

Ser Ser Phe Ser Glu Val Lys Pro Leu Leu Phe Asp His Leu Ala Gln
465 470 475 480

Leu Phe Phe Thr Ser Thr Ile Tyr Phe Lys Cys Ser Val Leu Gln Ser
485 490 495

Leu Lys Glu Leu Leu Gln Asn Trp Leu Leu Trp Leu Ser Met Asp Ile
500 505 510

His Met Lys Pro Val Thr Asn Ser Pro Leu Glu Thr Thr Leu Gly Gly
515 520 525

Ser Met Asn Cys Val Ser Lys Leu Ile His Tyr Val Gly Trp Leu Ser
530 535 540

Thr Thr Ala Met Arg Leu Glu Ser Asn Asn Thr Phe Leu Leu His Phe
545 550 555 560

Ile Leu Asp Phe Tyr Glu Lys Val Cys Asp Ile Tyr Ile Asn Tyr Asp
565 570 575

Leu Pro Leu Val Val Leu Phe Pro Pro Gly Ile Phe Tyr Ser Ala Leu
580 585 590

Leu Ser Leu Asp Thr Ser Ile Leu Asn Gln Leu Cys Phe Ile Met His
595 600 605

Arg Tyr Arg Lys Asn Leu Thr Ala Ala Lys Lys Asn Glu Leu Val Gln
610 615 620

Lys Thr Lys Ser Glu Phe Asn Phe Ser Ser Lys Thr Tyr Gln Glu Phe
625 630 635 640

Asn Tyr Tyr Leu Thr Ser Met Val Gly Cys Leu Trp Thr Ser Lys Pro
645 650 655

Phe Ala Lys Gly Ile Tyr Ile Asp Pro Glu Ile Leu Glu Lys Thr Gly
660 665 670

Val Ala Glu Tyr Lys Asn Ser Leu Asn Val Val His His Pro Ser Phe
675 680 685

Leu Ser Tyr Ala Val Ser Phe Leu Leu Gln Glu Ser Pro Glu Glu Arg
690 695 700

Thr Val Asn Val Ser Ser Ile Arg Gly Lys Lys Trp Ser Trp Tyr Leu
705 710 715 720

Asp Tyr Leu Phe Ser Gln Gly Leu Gln Gly Leu Lys Leu Phe Ile Arg
725 730 735

Ser Ser Val His His Ser Ser Ile Pro Arg Ala Glu Gly Ile Asn Cys
740 745 750

Asn Asn Gln Tyr
755

<210> 67
<211> 504
<212> PRT
<213> Homo sapiens

<400> 67

Met Glu Ala Pro Leu Gln Thr Glu Met Val Glu Leu Val Pro Asn Gly
1 5 10 15

Lys His Ser Glu Gly Leu Leu Pro Val Ile Thr Pro Met Ala Gly Asn
20 25 30

Gln Arg Val Glu Asp Pro Ala Arg Ser Cys Met Glu Gly Lys Ser Phe
35 40 45

Leu Gln Lys Ser Pro Ser Lys Glu Pro His Phe Thr Asp Phe Glu Gly
50 55 60

Lys Thr Ser Phe Gly Met Ser Val Phe Asn Leu Ser Asn Ala Ile Met
65 70 75 80

Gly Ser Gly Ile Leu Gly Leu Ala Tyr Ala Met Ala Asn Thr Gly Ile
85 90 95

Ile Leu Phe Leu Phe Leu Leu Thr Ala Val Ala Leu Leu Ser Ser Tyr
100 105 110

Ser Ile His Leu Leu Leu Lys Ser Ser Gly Val Val Gly Ile Arg Ala
115 120 125

Tyr Glu Gln Leu Gly Tyr Arg Ala Phe Gly Thr Pro Gly Lys Leu Ala
130 135 140

Ala Ala Leu Ala Ile Thr Leu Gln Asn Ile Gly Ala Met Ser Ser Tyr
145 150 155 160

Leu Tyr Ile Ile Lys Ser Glu Leu Pro Leu Val Ile Gln Thr Phe Leu
165 170 175

Asn Leu Glu Glu Lys Thr Ser Asp Trp Tyr Met Asn Gly Asn Tyr Leu
180 185 190

Val Ile Leu Val Ser Val Thr Ile Ile Leu Pro Leu Ala Leu Met Arg
195 200 205

Gln Leu Gly Tyr Leu Gly Tyr Ser Ser Gly Phe Ser Leu Ser Cys Met
210 215 220

Val Phe Phe Leu Ile Ala Val Ile Tyr Lys Lys Phe His Val Pro Cys
225 230 235 240

Pro Leu Pro Pro Asn Phe Asn Asn Thr Thr Gly Asn Phe Ser His Val
245 250 255

Glu Ile Val Lys Glu Lys Val Gln Leu Gln Val Glu Pro Glu Ala Ser
260 265 270

Ala Phe Cys Thr Pro Ser Tyr Phe Thr Leu Asn Ser Gln Thr Ala Tyr
275 280 285

Thr Ile Pro Ile Met Ala Phe Ala Phe Val Cys His Pro Glu Val Leu
290 295 300

Pro Ile Tyr Thr Glu Leu Lys Asp Pro Ser Lys Lys Lys Met Gln His
305 310 315 320

Ile Ser Asn Leu Ser Ile Ala Val Met Tyr Ile Met Tyr Phe Leu Ala
325 330 335

Ala Leu Phe Gly Tyr Leu Thr Phe Tyr Asn Gly Val Glu Ser Glu Leu
340 345 350

Leu His Thr Tyr Ser Lys Val Asp Pro Phe Asp Val Leu Ile Leu Cys
355 360 365

Val Arg Val Ala Val Leu Thr Ala Val Thr Leu Thr Val Pro Ile Val
370 375 380

Leu Phe Pro Val Arg Arg Ala Ile Gln Gln Met Leu Phe Pro Asn Gln
385 390 395 400

Glu Phe Ser Trp Leu Arg His Val Leu Ile Ala Val Gly Leu Leu Thr
405 410 415

Cys Ile Asn Leu Leu Val Ile Phe Ala Pro Asn Ile Leu Gly Ile Phe
420 425 430

Gly Val Ile Gly Ala Thr Ser Ala Pro Phe Leu Ile Phe Ile Phe Pro
435 440 445

Ala Ile Phe Tyr Phe Arg Ile Met Pro Thr Glu Lys Glu Pro Ala Arg
450 455 460

Ser Thr Pro Lys Ile Leu Ala Leu Cys Phe Ala Met Leu Gly Phe Leu
465 470 475 480

Leu Met Thr Met Ser Leu Ser Phe Ile Ile Ile Asp Trp Ala Ser Gly
485 490 495

Thr Ser Arg His Gly Gly Asn His
500

<210> 68
<211> 145
<212> PRT
<213> Homo sapiens

<400> 68

Met Ala Thr Trp Ala Leu Leu Leu Leu Ala Ala Met Leu Leu Gly Asn
1 5 10 15

Pro Gly Leu Val Phe Ser Arg Leu Ser Pro Glu Tyr Tyr Asp Leu Ala
20 25 30

Arg Ala His Leu Arg Asp Glu Glu Lys Ser Cys Pro Cys Leu Ala Gln
35 40 45

Glu Gly Pro Gln Gly Asp Leu Leu Thr Lys Thr Gln Glu Leu Gly Arg
50 55 60

Asp Tyr Arg Thr Cys Leu Thr Ile Val Gln Lys Leu Lys Lys Met Val
65 70 75 80

Asp Lys Pro Thr Gln Arg Ser Val Ser Asn Ala Ala Thr Arg Val Cys
85 90 95

Arg Thr Gly Arg Ser Arg Trp Arg Asp Val Cys Arg Asn Phe Met Arg
100 105 110

Arg Tyr Gln Ser Arg Val Ile Gln Gly Leu Val Ala Gly Glu Thr Ala
115 120 125

Gln Gln Ile Cys Glu Asp Leu Arg Leu Cys Ile Pro Ser Thr Gly Pro
130 135 140

Leu

145

<210> 69
<211> 128
<212> PRT
<213> Homo sapiens

<400> 69

Met Trp Ser Thr Arg Ser Pro Asn Ser Thr Ala Trp Pro Leu Ser Leu
1 5 10 15

Glu Pro Asp Pro Gly Met Ala Ser Ala Ser Thr Thr Met His Thr Thr
20 25 30

Thr Ile Ala Glu Pro Asp Pro Gly Met Ser Gly Trp Pro Asp Gly Arg
35 40 45

Met Glu Thr Ser Thr Pro Thr Ile Met Asp Ile Val Val Ile Ala Gly
50 55 60

Val Ile Ala Ala Val Ala Ile Val Leu Val Ser Leu Leu Phe Val Met
65 70 75 80

Leu Arg Tyr Met Tyr Arg His Lys Gly Thr Tyr His Thr Asn Glu Ala
85 90 95

Lys Gly Thr Glu Phe Ala Glu Ser Ala Asp Ala Ala Leu Gln Gly Asp
100 105 110

Pro Ala Leu Gln Asp Ala Gly Asp Ser Ser Arg Lys Glu Tyr Phe Ile
115 120 125

<210> 70
<211> 4861
<212> PRT
<213> Homo sapiens

<400> 70

Met Ala Thr Met Ile Pro Pro Val Lys Leu Lys Trp Leu Glu His Leu
1 5 10 15

Asn Ser Ser Trp Ile Thr Glu Asp Ser Glu Ser Ile Ala Thr Arg Glu
20 25 30

Gly Val Ala Val Leu Tyr Ser Lys Leu Val Ser Asn Lys Glu Val Val
35 40 45

Pro Leu Pro Gln Gln Val Leu Cys Leu Lys Gly Pro Gln Leu Pro Asp
50 55 60

Phe Glu Arg Glu Ser Leu Ser Ser Asp Glu Gln Asp His Tyr Leu Asp
65 70 75 80

Ala Leu Leu Ser Ser Gln Leu Ala Leu Ala Lys Met Val Cys Ser Asp
85 90 95

Ser Pro Phe Ala Gly Ala Leu Arg Lys Arg Leu Leu Val Leu Gln Arg
100 105 110

Val Phe Tyr Ala Leu Ser Asn Lys Tyr His Asp Lys Gly Lys Val Lys
115 120 125

Gln Gln Gln His Ser Pro Glu Ser Ser Ser Gly Ser Ala Asp Val His
130 135 140

Ser Val Ser Glu Arg Pro Arg Ser Ser Thr Asp Ala Leu Ile Glu Met
145 150 155 160

Gly Val Arg Thr Gly Leu Ser Leu Leu Phe Ala Leu Leu Arg Gln Ser
165 170 175

Trp Met Met Pro Val Ser Gly Pro Gly Leu Ser Leu Cys Asn Asp Val
180 185 190

Ile His Thr Ala Ile Glu Val Val Ser Ser Leu Pro Pro Leu Ser Leu
195 200 205

Ala Asn Glu Ser Lys Ile Pro Pro Met Gly Leu Asp Cys Leu Ser Gln
210 215 220

Val Thr Thr Phe Leu Lys Gly Val Thr Ile Pro Asn Ser Gly Ala Asp
225 230 235 240

Thr Leu Gly Arg Arg Leu Ala Ser Glu Leu Leu Leu Gly Leu Ala Ala
245 250 255

Gln Arg Gly Ser Leu Arg Tyr Leu Leu Glu Trp Ile Glu Met Ala Leu
260 265 270

Gly Ala Ser Ala Val Val His Thr Met Glu Lys Gly Lys Leu Leu Ser
275 280 285

Ser Gln Glu Gly Met Ile Ser Phe Asp Cys Phe Met Thr Ile Leu Met
290 295 300

Gln Met Arg Arg Ser Leu Gly Ser Ser Ala Asp Arg Ser Gln Trp Arg
305 310 315 320

Glu Pro Thr Arg Thr Ser Asp Gly Leu Cys Ser Leu Tyr Glu Ala Ala
325 330 335

Leu Cys Leu Phe Glu Glu Val Cys Arg Met Ala Ser Asp Tyr Ser Arg
340 345 350

Thr Cys Ala Ser Pro Asp Ser Ile Gln Thr Gly Asp Ala Pro Ile Val
355 360 365

Ser Glu Thr Cys Glu Val Tyr Val Trp Gly Ser Asn Ser Ser His Gln
370 375 380

Leu Val Glu Gly Thr Gln Glu Lys Ile Leu Gln Pro Lys Leu Ala Pro
385 390 395 400

Ser Phe Ser Asp Ala Gln Thr Ile Glu Ala Gly Gln Tyr Cys Thr Phe
405 410 415

Val Ile Ser Thr Asp Gly Ser Val Arg Ala Cys Gly Lys Gly Ser Tyr
420 425 430

Gly Arg Leu Gly Leu Gly Asp Ser Asn Asn Gln Ser Thr Leu Lys Lys
435 440 445

Leu Thr Phe Glu Pro His Arg Ser Ile Lys Lys Val Ser Ser Ser Lys
450 455 460

Gly Ser Asp Gly His Thr Leu Ala Phe Thr Thr Glu Gly Glu Val Phe
465 470 475 480

Ser Trp Gly Asp Gly Asp Tyr Gly Lys Leu Gly His Gly Asn Ser Ser
485 490 495

Thr Gln Lys Tyr Pro Lys Leu Ile Gln Gly Pro Leu Gln Gly Lys Val
500 505 510

Val Val Cys Val Ser Ala Gly Tyr Arg His Ser Ala Ala Val Thr Glu
515 520 525

Asp Gly Glu Leu Tyr Thr Trp Gly Glu Gly Asp Phe Gly Arg Leu Gly
530 535 540

His Gly Asp Ser Asn Ser Arg Asn Ile Pro Thr Leu Val Lys Asp Ile
545 550 555 560

Ser Asn Val Gly Glu Val Ser Cys Gly Ser Ser His Thr Ile Ala Leu
565 570 575

Ser Lys Asp Gly Arg Thr Val Trp Ser Phe Gly Gly Gly Asp Asn Gly
580 585 590

Lys Leu Gly His Gly Asp Thr Asn Arg Val Tyr Lys Pro Lys Val Ile
595 600 605

Glu Ala Leu Gln Gly Met Phe Ile Arg Lys Val Cys Ala Gly Ser Gln
610 615 620

Ser Ser Leu Ala Leu Thr Ser Thr Gly Gln Val Tyr Ala Trp Gly Cys
625 630 635 640

Gly Ala Cys Leu Gly Cys Gly Ser Ser Glu Ala Thr Ala Leu Arg Pro
645 650 655

Lys Leu Ile Glu Glu Leu Ala Ala Thr Arg Ile Val Asp Val Ser Ile
660 665 670

Gly Asp Ser His Cys Leu Ala Leu Ser His Asp Asn Glu Val Tyr Ala
675 680 685

Trp Gly Asn Asn Ser Met Gly Gln Cys Gly Gln Gly Asn Ser Thr Gly
690 695 700

Pro Ile Thr Lys Pro Lys Lys Val Ser Gly Leu Asp Gly Ile Ala Ile
705 710 715 720

Gln Gln Ile Ser Ala Gly Thr Ser His Ser Leu Ala Trp Thr Ala Leu
725 730 735

Pro Arg Asp Arg Gln Val Val Ala Trp His Arg Pro Tyr Cys Val Asp
740 745 750

Leu Glu Glu Ser Thr Phe Ser His Leu Arg Ser Phe Leu Glu Arg Tyr
755 760 765

Cys Asp Lys Ile Asn Ser Glu Ile Pro Pro Leu Pro Phe Pro Ser Ser
770 775 780

Arg Glu His His Ser Phe Leu Lys Leu Cys Leu Lys Leu Leu Ser Asn
785 790 795 800

His Leu Ala Leu Ala Leu Ala Gly Gly Val Ala Thr Ser Ile Leu Gly
805 810 815

Arg Gln Ala Gly Pro Leu Arg Asn Leu Leu Phe Arg Leu Met Asp Ser
820 825 830

Thr Val Pro Asp Glu Ile Gln Glu Val Val Ile Glu Thr Leu Ser Val
835 840 845

Gly Ala Thr Met Leu Leu Pro Pro Leu Arg Glu Arg Met Glu Leu Leu
850 855 860

His Ser Leu Leu Pro Gln Gly Pro Asp Arg Trp Glu Ser Leu Ser Lys
865 870 875 880

Gly Gln Arg Met Gln Leu Asp Ile Ile Leu Thr Ser Leu Gln Asp His
885 890 895

Thr His Val Ala Ser Leu Leu Gly Tyr Ser Ser Pro Ser Asp Ala Ala
900 905 910

Asp Leu Ser Ser Val Cys Thr Gly Tyr Gly Asn Leu Ser Asp Gln Pro
915 920 925

Tyr Gly Thr Gln Ser Cys His Pro Asp Thr His Leu Ala Glu Ile Leu
930 935 940

Met Lys Thr Leu Leu Arg Asn Leu Gly Phe Tyr Thr Asp Gln Ala Phe
945 950 955 960

Gly Glu Leu Glu Lys Asn Ser Asp Lys Phe Leu Leu Gly Thr Ser Ser
965 970 975

Ser Glu Asn Ser Gln Pro Ala His Leu His Glu Leu Leu Cys Ser Leu
980 985 990

Gln Lys Gln Leu Leu Ala Phe Cys His Ile Asn Asn Ile Ser Glu Asn
995 1000 1005

Ser Ser Ser Val Ala Leu Leu His Lys His Leu Gln Leu Leu Leu
1010 1015 1020

Pro His Ala Thr Asp Ile Tyr Ser Arg Ser Ala Asn Leu Leu Lys
1025 1030 1035

Glu Ser Pro Trp Asn Gly Ser Val Gly Glu Lys Leu Arg Asp Val
1040 1045 1050

Ile Tyr Val Ser Ala Ala Gly Ser Met Leu Cys Gln Ile Val Asn
1055 1060 1065

Ser Leu Leu Leu Leu Pro Val Ser Val Ala Arg Pro Leu Leu Ser
1070 1075 1080

Tyr Leu Leu Asp Leu Leu Pro Pro Leu Asp Cys Leu Asn Arg Leu
1085 1090 1095

Leu Pro Ala Ala Asp Leu Leu Glu Asp Gln Glu Leu Gln Trp Pro
1100 1105 1110

Leu His Gly Gly Pro Glu Leu Ile Asp Pro Ala Gly Leu Pro Leu
1115 1120 1125

Pro Gln Pro Ala Gln Ser Trp Val Trp Leu Val Asp Leu Glu Arg
1130 1135 1140

Thr Ile Ala Leu Leu Ile Gly Arg Cys Leu Gly Gly Met Leu Gln
1145 1150 1155

Gly Ser Pro Val Ser Pro Glu Glu Gln Asp Thr Ala Tyr Trp Met
1160 1165 1170

Lys Thr Pro Leu Phe Ser Asp Gly Val Glu Met Asp Thr Pro Gln
1175 1180 1185

Leu Asp Lys Cys Met Ser Cys Leu Leu Glu Val Ala Leu Ser Gly
1190 1195 1200

Asn Glu Glu Gln Lys Pro Phe Asp Tyr Lys Leu Arg Pro Glu Ile
1205 1210 1215

Ala Val Tyr Val Asp Leu Ala Leu Gly Cys Ser Lys Glu Pro Ala
1220 1225 1230

Arg Ser Leu Trp Ile Ser Met Gln Asp Tyr Ala Val Ser Lys Asp
1235 1240 1245

Trp Asp Ser Ala Thr Leu Ser Asn Glu Ser Leu Leu Asp Thr Val
1250 1255 1260

Ser Arg Phe Val Leu Ala Ala Leu Leu Lys His Thr Asn Leu Leu
1265 1270 1275

Ser Gln Ala Cys Gly Glu Ser Arg Tyr Gln Pro Gly Lys His Leu
1280 1285 1290

Ser Glu Val Tyr Arg Cys Val Tyr Lys Val Arg Ser Arg Leu Leu
1295 1300 1305

Ala Cys Lys Asn Leu Glu Leu Ile Gln Thr Arg Ser Ser Ser Arg
1310 1315 1320

Asp Arg Trp Ile Ser Glu Asn Gln Asp Ser Ala Asp Val Asp Pro
1325 1330 1335

Gln Glu His Ser Phe Thr Arg Thr Ile Asp Glu Glu Ala Glu Met
1340 1345 1350

Glu Glu Gln Ala Glu Arg Asp Arg Glu Glu Gly His Pro Glu Pro
1355 1360 1365

Glu Asp Glu Glu Glu Glu Arg Glu His Glu Val Met Thr Ala Gly
1370 1375 1380

Lys Ile Phe Gln Cys Phe Leu Ser Ala Arg Glu Val Ala Arg Ser
1385 1390 1395

Arg Asp Arg Asp Arg Met Asn Ser Gly Ala Gly Ser Gly Ala Arg
1400 1405 1410

Ala Asp Asp Pro Pro Pro Gln Ser Gln Gln Glu Arg Arg Val Ser
1415 1420 1425

Thr Asp Leu Pro Glu Gly Gln Asp Val Tyr Thr Ala Ala Cys Asn
1430 1435 1440

Ser Val Ile His Arg Cys Ala Leu Leu Ile Leu Gly Val Ser Pro
1445 1450 1455

Val Ile Asp Glu Leu Gln Lys Arg Arg Glu Glu Gly Gln Leu Gln
1460 1465 1470

Gln Pro Ser Thr Ser Ala Ser Glu Gly Gly Gly Leu Met Thr Arg
1475 1480 1485

Ser Glu Ser Leu Thr Ala Glu Ser Arg Leu Val His Thr Ser Pro
1490 1495 1500

Asn Tyr Arg Leu Ile Lys Ser Arg Ser Glu Ser Asp Leu Ser Gln
1505 1510 1515

Pro Glu Ser Asp Glu Glu Gly Tyr Ala Leu Ser Gly Arg Gln Asn
1520 1525 1530

Val Asp Leu Asp Leu Ala Ala Ser His Arg Lys Arg Gly Pro Met
1535 1540 1545

His Ser Gln Leu Glu Ser Leu Ser Asp Ser Trp Ala Arg Leu Lys
1550 1555 1560

His Ser Arg Asp Trp Leu Cys Asn Ser Ser Tyr Ser Phe Glu Ser
1565 1570 1575

Asp Phe Asp Leu Thr Lys Ser Leu Gly Val His Thr Leu Ile Glu
1580 1585 1590

Asn Val Val Ser Phe Val Ser Gly Asp Val Gly Asn Ala Pro Gly
1595 1600 1605

Phe Lys Glu Pro Glu Glu Ser Met Ser Thr Ser Pro Gln Ala Ser
1610 1615 1620

Ile Ile Ala Met Glu Gln Gln Gln Leu Arg Ala Glu Leu Arg Leu
1625 1630 1635

Glu Ala Leu His Gln Ile Leu Val Leu Leu Ser Gly Met Glu Glu
1640 1645 1650

Lys Gly Ser Ile Ser Leu Ala Gly Ser Arg Leu Ser Ser Gly Phe
1655 1660 1665

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Gln Ser  Ser Thr Leu Leu Thr  Ser Val Arg Leu Gln  Phe Leu Ala
    1670                 1675                 1680

Gly Cys  Phe Gly Leu Gly Thr  Val Gly His Thr Gly  Ala Lys Gly
    1685                 1690                 1695

Glu Ser  Gly Arg Leu His His  Tyr Gln Asp Gly Ile  Arg Ala Ala
    1700                 1705                 1710

Lys Arg  Asn Ile Gln Ile Glu  Ile Gln Val Ala Val  His Lys Ile
    1715                 1720                 1725

Tyr Gln  Gln Leu Ser Ala Thr  Leu Glu Arg Ala Leu  Gln Ala Asn
    1730                 1735                 1740

Lys His  His Ile Glu Ala Gln  Gln Arg Leu Leu Leu  Val Thr Val
    1745                 1750                 1755

Phe Ala  Leu Ser Val His Tyr  Gln Pro Val Asp Val  Ser Leu Ala
    1760                 1765                 1770

Ile Ser  Thr Gly Leu Leu Asn  Val Leu Ser Gln Leu  Cys Gly Thr
    1775                 1780                 1785

Asp Thr  Met Leu Gly Gln Pro  Leu Gln Leu Leu Pro  Lys Thr Gly
    1790                 1795                 1800

Val Ser  Gln Leu Ser Thr Ala  Leu Lys Val Ala Ser  Thr Arg Leu
    1805                 1810                 1815

Leu Gln  Ile Leu Ala Ile Thr  Thr Gly Thr Tyr Ala  Asp Lys Leu
    1820                 1825                 1830

Ser Pro  Lys Val Val Gln Ser  Leu Leu Asp Leu Leu  Cys Ser Gln
    1835                 1840                 1845

Leu Lys  Asn Leu Leu Ser Gln  Thr Gly Val Leu His  Met Ala Ser
    1850                 1855                 1860

Phe Gly  Glu Gly Glu Gln Glu  Asp Gly Glu Glu Glu  Glu Lys Lys
    1865                 1870                 1875

Val Asp  Ser Ser Gly Glu Thr  Glu Lys Lys Asp Phe  Arg Ala Ala
    1880                 1885                 1890

Leu Arg  Lys Gln His Ala Ala  Glu Leu His Leu Gly  Asp Phe Leu
    1895                 1900                 1905

Val Phe  Leu Arg Arg Val Val  Ser Ser Lys Ala Ile  Gln Ser Lys
    1910                 1915                 1920

Met Ala  Ser Pro Lys Trp Thr  Glu Val Leu Leu Asn  Ile Ala Ser
    1925                 1930                 1935

Gln Lys  Cys Ser Ser Gly Ile  Pro Leu Val Gly Asn  Leu Arg Thr
    1940                 1945                 1950

Arg Leu  Leu Ala Leu His Val  Leu Glu Ala Val Leu  Pro Ala Cys
    1955                 1960                 1965
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Glu Ser  Gly Val Glu Asp Asp  Gln Met Ala Gln Ile  Val Glu Arg
    1970                 1975                 1980

Leu Phe  Ser Leu Leu Ser Asp  Cys Met Trp Glu Thr  Pro Ile Ala
    1985                 1990                 1995

Gln Ala  Lys His Ala Ile Gln  Ile Lys Glu Lys Glu  Gln Glu Ile
    2000                 2005                 2010

Lys Leu  Gln Lys Gln Gly Glu  Leu Glu Glu Glu Asp  Glu Asn Leu
    2015                 2020                 2025

Pro Ile  Gln Glu Val Ser Phe  Asp Pro Glu Lys Ala  Gln Cys Cys
    2030                 2035                 2040

Leu Val  Glu Asn Gly Gln Ile  Leu Thr His Gly Ser  Gly Gly Lys
    2045                 2050                 2055

Gly Tyr  Gly Leu Ala Ser Thr  Gly Val Thr Ser Gly  Cys Tyr Gln
    2060                 2065                 2070

Trp Lys  Phe Tyr Ile Val Lys  Glu Asn Arg Gly Asn  Glu Gly Thr
    2075                 2080                 2085

Cys Val  Gly Val Ser Arg Trp  Pro Val His Asp Phe  Asn His Arg
    2090                 2095                 2100

Thr Thr  Ser Asp Met Trp Leu  Tyr Arg Ala Tyr Ser  Gly Asn Leu
    2105                 2110                 2115

Tyr His  Asn Gly Glu Gln Thr  Leu Thr Leu Ser Ser  Phe Thr Gln
    2120                 2125                 2130

Gly Asp  Phe Ile Thr Cys Val  Leu Asp Met Glu Ala  Arg Thr Ile
    2135                 2140                 2145

Ser Phe  Gly Lys Asn Gly Glu  Glu Pro Lys Leu Ala  Phe Glu Asp
    2150                 2155                 2160

Val Asp  Ala Ala Glu Leu Tyr  Pro Cys Val Met Phe  Tyr Ser Ser
    2165                 2170                 2175

Asn Pro  Gly Glu Lys Val Lys  Ile Cys Asp Met Gln  Met Arg Gly
    2180                 2185                 2190

Thr Pro  Arg Asp Leu Leu Pro  Gly Asp Pro Ile Cys  Ser Pro Val
    2195                 2200                 2205

Ala Ala  Val Leu Ala Glu Ala  Thr Ile Gln Leu Val  Arg Ile Leu
    2210                 2215                 2220

His Arg  Thr Asp Arg Trp Thr  Tyr Cys Ile Asn Lys  Lys Met Met
    2225                 2230                 2235

Glu Arg  Leu His Lys Ile Lys  Ile Cys Ile Lys Glu  Ser Gly Gln
    2240                 2245                 2250

Lys Leu  Lys Lys Ser Arg Ser  Val Gln Ser Arg Glu  Glu Asn Glu
    2255                 2260                 2265
```

Met Arg Glu Glu Lys Glu Ser Lys Glu Glu Glu Lys Gly Lys His
2270 2275 2280

Thr Arg His Gly Leu Ala Asp Leu Ser Glu Leu Gln Leu Arg Thr
2285 2290 2295

Leu Cys Ile Glu Val Trp Pro Val Leu Ala Val Ile Gly Gly Val
2300 2305 2310

Asp Ala Gly Leu Arg Val Gly Gly Arg Cys Val His Lys Gln Thr
2315 2320 2325

Gly Arg His Ala Thr Leu Leu Gly Val Val Lys Glu Gly Ser Thr
2330 2335 2340

Ser Ala Lys Val Gln Trp Asp Glu Ala Glu Ile Thr Ile Ser Phe
2345 2350 2355

Pro Thr Phe Trp Ser Pro Ser Asp Thr Pro Leu Tyr Asn Leu Glu
2360 2365 2370

Pro Cys Glu Pro Leu Pro Phe Asp Val Ala Arg Phe Arg Gly Leu
2375 2380 2385

Thr Ala Ser Val Leu Leu Asp Leu Thr Tyr Leu Thr Gly Val His
2390 2395 2400

Glu Asp Met Gly Lys Gln Ser Thr Lys Arg His Glu Lys Lys His
2405 2410 2415

Arg His Glu Ser Glu Glu Lys Gly Asp Val Glu Gln Lys Pro Glu
2420 2425 2430

Ser Glu Ser Ala Leu Asp Met Arg Thr Gly Leu Thr Ser Asp Asp
2435 2440 2445

Val Lys Ser Gln Ser Thr Thr Ser Ser Lys Ser Glu Asn Glu Ile
2450 2455 2460

Ala Ser Phe Ser Leu Asp Pro Thr Leu Pro Ser Val Glu Ser Gln
2465 2470 2475

His Gln Ile Thr Glu Gly Lys Arg Lys Asn His Glu His Met Ser
2480 2485 2490

Lys Asn His Asp Val Ala Gln Ser Glu Ile Arg Ala Val Gln Leu
2495 2500 2505

Ser Tyr Leu Tyr Leu Gly Ala Met Lys Ser Leu Ser Ala Leu Leu
2510 2515 2520

Gly Cys Ser Lys Tyr Ala Glu Leu Leu Leu Ile Pro Lys Val Leu
2525 2530 2535

Ala Glu Asn Gly His Asn Ser Asp Cys Ala Ser Ser Pro Val Val
2540 2545 2550

His Glu Asp Val Glu Met Arg Ala Ala Leu Gln Phe Leu Met Arg
2555 2560 2565

```
His Met  Val Lys Arg Ala Val  Met Arg Ser Pro Ile  Lys Arg Ala
    2570                 2575                 2580

Leu Gly  Leu Ala Asp Leu Glu  Arg Ala Gln Ala Met  Ile Tyr Lys
    2585                 2590                 2595

Leu Val  Val His Gly Leu Leu  Glu Asp Gln Phe Gly  Gly Lys Ile
    2600                 2605                 2610

Lys Gln  Glu Ile Asp Gln Gln  Ala Glu Glu Ser Asp  Pro Ala Gln
    2615                 2620                 2625

Gln Ala  Gln Thr Pro Val Thr  Thr Ser Pro Ser Ala  Ser Ser Thr
    2630                 2635                 2640

Thr Ser  Phe Met Ser Ser Ser  Leu Glu Asp Thr Thr  Thr Ala Thr
    2645                 2650                 2655

Thr Pro  Val Thr Asp Thr Glu  Thr Val Pro Ala Ser  Glu Ser Pro
    2660                 2665                 2670

Gly Val  Met Pro Leu Ser Leu  Leu Arg Gln Met Phe  Ser Ser Tyr
    2675                 2680                 2685

Pro Thr  Thr Thr Val Leu Pro  Thr Arg Arg Ala Gln  Thr Pro Pro
    2690                 2695                 2700

Ile Ser  Ser Leu Pro Thr Ser  Pro Ser Asp Glu Val  Gly Arg Arg
    2705                 2710                 2715

Gln Ser  Leu Thr Ser Pro Asp  Ser Gln Ser Ala Arg  Pro Ala Asn
    2720                 2725                 2730

Arg Thr  Ala Leu Ser Asp Pro  Ser Ser Arg Leu Ser  Thr Ser Pro
    2735                 2740                 2745

Pro Pro  Pro Ala Ile Ala Val  Pro Leu Leu Glu Met  Gly Phe Ser
    2750                 2755                 2760

Leu Arg  Gln Ile Ala Lys Ala  Met Glu Ala Thr Gly  Ala Arg Gly
    2765                 2770                 2775

Glu Ala  Asp Ala Gln Asn Ile  Thr Val Leu Ala Met  Trp Met Ile
    2780                 2785                 2790

Glu His  Pro Gly His Glu Asp  Glu Glu Glu Pro Gln  Ser Gly Ser
    2795                 2800                 2805

Thr Ala  Asp Ser Arg Pro Gly  Ala Ala Val Leu Gly  Ser Gly Gly
    2810                 2815                 2820

Lys Ser  Asn Asp Pro Cys Tyr  Leu Gln Ser Pro Gly  Asp Ile Pro
    2825                 2830                 2835

Ser Ala  Asp Ala Ala Glu Met  Glu Glu Gly Phe Ser  Glu Ser Pro
    2840                 2845                 2850

Asp Asn  Leu Asp His Thr Glu  Asn Ala Ala Ser Gly  Ser Gly Pro
    2855                 2860                 2865
```

Ser Ala Arg Gly Arg Ser Ala Val Thr Arg Arg His Lys Phe Asp
2870 2875 2880

Leu Ala Ala Arg Thr Leu Leu Ala Arg Ala Ala Gly Leu Tyr Arg
2885 2890 2895

Ser Val Gln Ala His Arg Asn Gln Ser Arg Arg Glu Gly Ile Ser
2900 2905 2910

Leu Gln Gln Asp Pro Gly Ala Leu Tyr Asp Phe Asn Leu Asp Glu
2915 2920 2925

Glu Leu Glu Ile Asp Leu Asp Asp Glu Ala Met Glu Ala Met Phe
2930 2935 2940

Gly Gln Asp Leu Thr Ser Asp Asn Asp Ile Leu Gly Met Trp Ile
2945 2950 2955

Pro Glu Val Leu Asp Trp Pro Thr Trp His Val Cys Glu Ser Glu
2960 2965 2970

Asp Arg Glu Glu Val Val Val Cys Glu Leu Cys Glu Cys Ser Val
2975 2980 2985

Val Ser Phe Asn Gln His Met Lys Arg Asn His Pro Gly Cys Gly
2990 2995 3000

Arg Ser Ala Asn Arg Gln Gly Tyr Arg Ser Asn Gly Ser Tyr Val
3005 3010 3015

Asp Gly Trp Phe Gly Gly Glu Cys Gly Ser Gly Asn Pro Tyr Tyr
3020 3025 3030

Leu Leu Cys Gly Thr Cys Arg Glu Lys Tyr Leu Ala Met Lys Thr
3035 3040 3045

Lys Ser Lys Ser Thr Ser Ser Glu Arg Tyr Lys Gly Gln Ala Pro
3050 3055 3060

Asp Leu Ile Gly Lys Gln Asp Ser Val Tyr Glu Glu Asp Trp Asp
3065 3070 3075

Met Leu Asp Val Asp Glu Asp Glu Lys Leu Thr Gly Glu Glu Glu
3080 3085 3090

Phe Glu Leu Leu Ala Gly Pro Leu Gly Leu Asn Asp Arg Arg Ile
3095 3100 3105

Val Pro Glu Pro Val Gln Phe Pro Asp Ser Asp Pro Leu Gly Ala
3110 3115 3120

Ser Val Ala Met Val Thr Ala Thr Asn Ser Met Glu Glu Thr Leu
3125 3130 3135

Met Gln Ile Gly Cys His Gly Ser Val Glu Lys Ser Ser Ser Gly
3140 3145 3150

Arg Ile Thr Leu Gly Glu Gln Ala Ala Ala Leu Ala Asn Pro His
3155 3160 3165

Asp Arg Val Val Ala Leu Arg Arg Val Thr Ala Ala Ala Gln Val
3170 3175 3180

Leu Leu Ala Arg Thr Met Val Met Arg Ala Leu Ser Leu Leu Ser
3185 3190 3195

Val Ser Gly Ser Ser Cys Ser Leu Ala Ala Gly Leu Glu Ser Leu
3200 3205 3210

Gly Leu Thr Asp Ile Arg Thr Leu Val Arg Leu Met Cys Leu Ala
3215 3220 3225

Ala Ala Gly Arg Ala Gly Leu Ser Thr Ser Pro Ser Ala Met Ala
3230 3235 3240

Ser Thr Ser Glu Arg Ser Arg Gly Gly His Ser Lys Ala Asn Lys
3245 3250 3255

Pro Ile Ser Cys Leu Ala Tyr Leu Ser Thr Ala Val Gly Cys Leu
3260 3265 3270

Ala Ser Asn Ala Pro Ser Ala Ala Lys Leu Leu Val Gln Leu Cys
3275 3280 3285

Thr Gln Asn Leu Ile Ser Ala Ala Thr Gly Val Asn Leu Thr Thr
3290 3295 3300

Val Asp Asp Ser Ile Gln Arg Lys Phe Leu Pro Ser Phe Leu Arg
3305 3310 3315

Gly Ile Ala Glu Glu Asn Lys Leu Val Thr Ser Pro Asn Phe Val
3320 3325 3330

Val Thr Gln Ala Leu Val Ala Leu Leu Ala Asp Lys Gly Ala Lys
3335 3340 3345

Leu Arg Pro Asn Tyr Asp Lys Ser Glu Val Glu Lys Lys Gly Pro
3350 3355 3360

Leu Glu Leu Ala Asn Ala Leu Ala Ala Cys Cys Leu Ser Ser Arg
3365 3370 3375

Leu Ser Ser Gln His Arg Gln Trp Ala Ala Gln Gln Leu Val Arg
3380 3385 3390

Thr Leu Ala Ala His Asp Arg Asp Asn Gln Thr Thr Leu Gln Thr
3395 3400 3405

Leu Ala Asp Met Gly Gly Asp Leu Arg Lys Cys Ser Phe Ile Lys
3410 3415 3420

Leu Glu Ala His Gln Asn Arg Val Met Thr Cys Val Trp Cys Asn
3425 3430 3435

Lys Lys Gly Leu Leu Ala Thr Ser Gly Asn Asp Gly Thr Ile Arg
3440 3445 3450

Val Trp Asn Val Thr Lys Lys Gln Tyr Ser Leu Gln Gln Thr Cys
3455 3460 3465

Val Phe Asn Arg Leu Glu Gly Asp Ala Glu Glu Ser Leu Gly Ser
3470 3475 3480

Pro Ser Asp Pro Ser Phe Ser Pro Val Ser Trp Ser Ile Ser Gly
3485 3490 3495

Lys Tyr Leu Ala Gly Ala Leu Glu Lys Met Val Asn Ile Trp Gln
3500 3505 3510

Val Asn Gly Gly Lys Gly Leu Val Asp Ile Gln Pro His Trp Val
3515 3520 3525

Ser Ala Leu Ala Trp Pro Glu Glu Gly Pro Ala Thr Ala Trp Ser
3530 3535 3540

Gly Glu Ser Pro Glu Leu Leu Leu Val Gly Arg Met Asp Gly Ser
3545 3550 3555

Leu Gly Leu Ile Glu Val Val Asp Val Ser Thr Met His Arg Arg
3560 3565 3570

Glu Leu Glu His Cys Tyr Arg Lys Asp Val Ser Val Thr Cys Ile
3575 3580 3585

Ala Trp Phe Ser Glu Asp Arg Pro Phe Ala Val Gly Tyr Phe Asp
3590 3595 3600

Gly Lys Leu Leu Leu Gly Thr Lys Glu Pro Leu Glu Lys Gly Gly
3605 3610 3615

Ile Val Leu Ile Asp Ala His Lys Asp Thr Leu Ile Ser Met Lys
3620 3625 3630

Trp Asp Pro Thr Gly His Ile Leu Met Thr Cys Ala Lys Glu Asp
3635 3640 3645

Ser Val Lys Leu Trp Gly Ser Ile Ser Gly Cys Trp Cys Cys Leu
3650 3655 3660

His Ser Leu Cys His Pro Ser Ile Val Asn Gly Ile Ala Trp Cys
3665 3670 3675

Arg Leu Pro Gly Lys Gly Ser Lys Leu Gln Leu Leu Met Ala Thr
3680 3685 3690

Gly Cys Gln Ser Gly Leu Val Cys Val Trp Arg Ile Pro Gln Asp
3695 3700 3705

Thr Thr Gln Thr Asn Val Thr Ser Ala Glu Gly Trp Trp Asp Gln
3710 3715 3720

Glu Ser Asn Cys Gln Asp Gly Tyr Arg Lys Ser Ser Gly Ala Lys
3725 3730 3735

Cys Val Tyr Gln Leu Arg Gly His Ile Thr Pro Val Arg Thr Val
3740 3745 3750

Ala Phe Ser Ser Asp Gly Leu Ala Leu Val Ser Gly Gly Leu Gly
3755 3760 3765

Gly Leu Met Asn Ile Trp Ser Leu Arg Asp Gly Ser Val Leu Gln
3770 3775 3780

Thr Val Val Ile Gly Ser Gly Ala Ile Gln Thr Thr Val Trp Ile
3785 3790 3795

Pro Glu Val Gly Val Ala Ala Cys Ser Asn Arg Ser Lys Asp Val
3800 3805 3810

Leu Val Val Asn Cys Thr Ala Glu Trp Ala Ala Ala Asn His Val
3815 3820 3825

Leu Ala Thr Cys Arg Thr Ala Leu Lys Gln Gln Gly Val Leu Gly
3830 3835 3840

Leu Asn Met Ala Pro Cys Met Arg Ala Phe Leu Glu Arg Leu Pro
3845 3850 3855

Met Met Leu Gln Glu Gln Tyr Ala Tyr Glu Lys Pro His Val Val
3860 3865 3870

Cys Gly Asp Gln Leu Val His Ser Pro Tyr Met Gln Cys Leu Ala
3875 3880 3885

Ser Leu Ala Val Gly Leu His Leu Asp Gln Leu Leu Cys Asn Pro
3890 3895 3900

Pro Val Pro Pro His His Gln Asn Cys Leu Pro Asp Pro Ala Ser
3905 3910 3915

Trp Asn Pro Asn Glu Trp Ala Trp Leu Glu Cys Phe Ser Thr Thr
3920 3925 3930

Ile Lys Ala Ala Glu Ala Leu Thr Asn Gly Ala Gln Phe Pro Glu
3935 3940 3945

Ser Phe Thr Val Pro Asp Leu Glu Pro Val Pro Glu Asp Glu Leu
3950 3955 3960

Val Phe Leu Met Asp Asn Ser Lys Trp Ile Asn Gly Met Asp Glu
3965 3970 3975

Gln Ile Met Ser Trp Ala Thr Ser Arg Pro Glu Asp Trp His Leu
3980 3985 3990

Gly Gly Lys Cys Asp Val Tyr Leu Trp Gly Ala Gly Arg His Gly
3995 4000 4005

Gln Leu Ala Glu Ala Gly Arg Asn Val Met Val Pro Ala Ala Ala
4010 4015 4020

Pro Ser Phe Ser Gln Ala Gln Gln Val Ile Cys Gly Gln Asn Cys
4025 4030 4035

Thr Phe Val Ile Gln Ala Asn Gly Thr Val Leu Ala Cys Gly Glu
4040 4045 4050

Gly Ser Tyr Gly Arg Leu Gly Gln Gly Asn Ser Asp Asp Leu His
4055 4060 4065

Val Leu Thr Val Ile Ser Ala Leu Gln Gly Phe Val Val Thr Gln
4070 4075 4080

Leu Val Thr Ser Cys Gly Ser Asp Gly His Ser Met Ala Leu Thr
4085 4090 4095

Glu Ser Gly Glu Val Phe Ser Trp Gly Asp Gly Asp Tyr Gly Lys
4100 4105 4110

Leu Gly His Gly Asn Ser Asp Arg Gln Arg Arg Pro Arg Gln Ile
4115 4120 4125

Glu Ala Leu Gln Gly Glu Glu Val Val Gln Met Ser Cys Gly Phe
4130 4135 4140

Lys His Ser Ala Val Val Thr Ser Asp Gly Lys Leu Phe Thr Phe
4145 4150 4155

Gly Asn Gly Asp Tyr Gly Arg Leu Gly Leu Gly Asn Thr Ser Asn
4160 4165 4170

Lys Lys Leu Pro Glu Arg Val Thr Ala Leu Glu Gly Tyr Gln Ile
4175 4180 4185

Gly Gln Val Ala Cys Gly Leu Asn His Thr Leu Ala Val Ser Ala
4190 4195 4200

Asp Gly Ser Met Val Trp Ala Phe Gly Asp Gly Asp Tyr Gly Lys
4205 4210 4215

Leu Gly Leu Gly Asn Ser Thr Ala Lys Ser Ser Pro Gln Lys Ile
4220 4225 4230

Asp Val Leu Cys Gly Ile Gly Ile Lys Lys Val Ala Cys Gly Thr
4235 4240 4245

Gln Phe Ser Val Ala Leu Thr Lys Asp Gly His Val Tyr Thr Phe
4250 4255 4260

Gly Gln Asp Arg Leu Ile Gly Leu Pro Glu Gly Arg Ala Arg Asn
4265 4270 4275

His Asn Arg Pro Gln Gln Ile Pro Val Leu Ala Gly Val Ile Ile
4280 4285 4290

Glu Asp Val Ala Val Gly Ala Glu His Thr Leu Ala Leu Ala Ser
4295 4300 4305

Asn Gly Asp Val Tyr Ala Trp Gly Ser Asn Ser Glu Gly Gln Leu
4310 4315 4320

Gly Leu Gly His Thr Asn His Val Arg Glu Pro Thr Leu Val Thr
4325 4330 4335

Gly Leu Gln Gly Lys Asn Val Arg Gln Ile Ser Ala Gly Arg Cys
4340 4345 4350

His Ser Ala Ala Trp Thr Ala Pro Pro Val Pro Pro Arg Ala Pro
4355 4360 4365

Gly Val Ser Val Pro Leu Gln Leu Gly Leu Pro Asp Thr Val Pro
4370 4375 4380

Pro Gln Tyr Gly Ala Leu Arg Glu Val Ser Ile His Thr Val Arg
4385 4390 4395

Ala Arg Leu Arg Leu Leu Tyr His Phe Ser Asp Leu Met Tyr Ser
4400 4405 4410

Ser Trp Arg Leu Leu Asn Leu Ser Pro Asn Asn Gln Asn Ser Thr
4415 4420 4425

Ser His Tyr Asn Ala Gly Thr Trp Gly Ile Val Gln Gly Gln Leu
4430 4435 4440

Arg Pro Leu Leu Ala Pro Arg Val Tyr Thr Leu Pro Met Val Arg
4445 4450 4455

Ser Ile Gly Lys Thr Met Val Gln Gly Lys Asn Tyr Gly Pro Gln
4460 4465 4470

Ile Thr Val Lys Arg Ile Ser Thr Arg Gly Arg Lys Cys Lys Pro
4475 4480 4485

Ile Phe Val Gln Ile Ala Arg Gln Val Val Lys Leu Asn Ala Ser
4490 4495 4500

Asp Leu Arg Leu Pro Ser Arg Ala Trp Lys Val Lys Leu Val Gly
4505 4510 4515

Glu Gly Ala Asp Asp Ala Gly Gly Val Phe Asp Asp Thr Ile Thr
4520 4525 4530

Glu Met Cys Gln Glu Leu Glu Thr Gly Ile Val Asp Leu Leu Ile
4535 4540 4545

Pro Ser Pro Asn Ala Thr Ala Glu Val Gly Tyr Asn Arg Asp Arg
4550 4555 4560

Phe Leu Phe Asn Pro Ser Ala Cys Leu Asp Glu His Leu Met Gln
4565 4570 4575

Phe Lys Phe Leu Gly Ile Leu Met Gly Val Ala Ile Arg Thr Lys
4580 4585 4590

Lys Pro Leu Asp Leu His Leu Ala Pro Leu Val Trp Lys Gln Leu
4595 4600 4605

Cys Cys Val Pro Leu Thr Leu Glu Asp Leu Glu Glu Val Asp Leu
4610 4615 4620

Leu Tyr Val Gln Thr Leu Asn Ser Ile Leu His Ile Glu Asp Ser
4625 4630 4635

Gly Ile Thr Glu Glu Ser Phe His Glu Met Ile Pro Leu Asp Ser
4640 4645 4650

Phe Val Gly Gln Ser Ala Asp Gly Lys Met Val Pro Ile Ile Pro
4655 4660 4665

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Gly Gly  Asn Ser Ile Pro Leu  Thr Phe Ser Asn Arg  Lys Glu Tyr
    4670                 4675                 4680

Val Glu  Arg Ala Ile Glu Tyr  Arg Leu His Glu Met  Asp Arg Gln
    4685                 4690                 4695

Val Ala  Ala Val Arg Glu Gly  Met Ser Trp Ile Val  Pro Val Pro
    4700                 4705                 4710

Leu Leu  Ser Leu Leu Thr Ala  Lys Gln Leu Glu Gln  Met Val Cys
    4715                 4720                 4725

Gly Met  Pro Glu Ile Ser Val  Glu Val Leu Lys Lys  Val Val Arg
    4730                 4735                 4740

Tyr Arg  Glu Val Asp Glu Gln  His Gln Leu Val Gln  Trp Phe Trp
    4745                 4750                 4755

His Thr  Leu Glu Glu Phe Ser  Asn Glu Glu Arg Val  Leu Phe Met
    4760                 4765                 4770

Arg Phe  Val Ser Gly Arg Ser  Arg Leu Pro Ala Asn  Thr Ala Asp
    4775                 4780                 4785

Ile Ser  Gln Arg Phe Gln Ile  Met Lys Val Asp Arg  Pro Tyr Asp
    4790                 4795                 4800

Ser Leu  Pro Thr Ser Gln Thr  Cys Phe Phe Gln Leu  Arg Leu Pro
    4805                 4810                 4815

Pro Tyr  Ser Ser Gln Leu Val  Met Ala Glu Arg Leu  Arg Tyr Ala
    4820                 4825                 4830

Ile Asn  Asn Cys Arg Ser Ile  Asp Met Asp Asn Tyr  Met Leu Ser
    4835                 4840                 4845

Arg Asn  Val Asp Asn Ala Glu  Gly Ser Asp Thr Asp  Tyr
    4850                 4855                 4860

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<212>  PRT
<213>  Homo sapiens

<400>  71

Met Ala Ser Ser Met Arg Ser Leu Phe Ser Asp His Gly Lys Tyr Val
1               5                  10                  15

Glu Ser Phe Arg Arg Phe Leu Asn His Ser Thr Glu His Gln Cys Met
            20                  25                  30

Gln Glu Phe Met Asp Lys Lys Leu Pro Gly Ile Ile Gly Arg Ile Gly
        35                  40                  45

Asp Thr Lys Ser Glu Ile Lys Ile Leu Ser Ile Gly Gly Gly Ala Gly
    50                  55                  60

Glu Ile Asp Leu Gln Ile Leu Ser Lys Val Gln Ala Gln Tyr Pro Gly
```

65 70 75 80

Val Cys Ile Asn Asn Glu Val Val Glu Pro Ser Ala Glu Gln Ile Ala
85 90 95

Lys Tyr Lys Glu Leu Val Ala Lys Thr Ser Asn Leu Glu Asn Val Lys
100 105 110

Phe Ala Trp His Lys Glu Thr Ser Ser Glu Tyr Gln Ser Arg Met Leu
115 120 125

Glu Lys Lys Glu Leu Gln Lys Trp Asp Phe Ile His Met Ile Gln Met
130 135 140

Leu Tyr Tyr Val Lys Asp Ile Pro Ala Thr Leu Lys Phe Phe His Ser
145 150 155 160

Leu Leu Gly Thr Asn Ala Lys Met Leu Ile Ile Val Val Ser Gly Ser
165 170 175

Ser Gly Trp Asp Lys Leu Trp Lys Lys Tyr Gly Ser Arg Phe Pro Gln
180 185 190

Asp Asp Leu Cys Gln Tyr Ile Thr Ser Asp Asp Leu Thr Gln Met Leu
195 200 205

Asp Asn Leu Gly Leu Lys Tyr Glu Cys Tyr Asp Leu Leu Ser Thr Met
210 215 220

Asp Ile Ser Asp Cys Phe Ile Asp Gly Asn Glu Asn Gly Asp Leu Leu
225 230 235 240

Trp Asp Phe Leu Thr Glu Thr Cys Asn Phe Asn Ala Thr Ala Pro Pro
245 250 255

Asp Leu Arg Ala Glu Leu Gly Lys Asp Leu Gln Glu Pro Glu Phe Ser
260 265 270

Ala Lys Lys Glu Gly Lys Val Leu Phe Asn Asn Thr Leu Ser Phe Ile
275 280 285

Val Ile Glu Ala
290

<210> 72
<211> 481
<212> PRT
<213> Homo sapiens

<400> 72

Met Ala Leu Ser Tyr Arg Val Ser Glu Leu Gln Ser Thr Ile Pro Glu
1 5 10 15

His Ile Leu Gln Ser Thr Phe Val His Val Ile Ser Ser Asn Trp Ser
20 25 30

Gly Leu Gln Thr Glu Ser Ile Pro Glu Glu Met Lys Gln Ile Val Glu
35 40 45

Glu Gln Gly Asn Lys Leu His Trp Ala Ala Leu Leu Ile Leu Met Val
50 55 60

Ile Ile Pro Thr Ile Gly Gly Asn Thr Leu Val Ile Leu Ala Val Ser
65 70 75 80

Leu Glu Lys Lys Leu Gln Tyr Ala Thr Asn Tyr Phe Leu Met Ser Leu
85 90 95

Ala Val Ala Asp Leu Leu Val Gly Leu Phe Val Met Pro Ile Ala Leu
100 105 110

Leu Thr Ile Met Phe Glu Ala Met Trp Pro Leu Pro Leu Val Leu Cys
115 120 125

Pro Ala Trp Leu Phe Leu Asp Val Leu Phe Ser Thr Ala Ser Ile Met
130 135 140

His Leu Cys Ala Ile Ser Val Asp Arg Tyr Ile Ala Ile Lys Lys Pro
145 150 155 160

Ile Gln Ala Asn Gln Tyr Asn Ser Arg Ala Thr Ala Phe Ile Lys Ile
165 170 175

Thr Val Val Trp Leu Ile Ser Ile Gly Ile Ala Ile Pro Val Pro Ile
180 185 190

Lys Gly Ile Glu Thr Asp Val Asp Asn Pro Asn Asn Ile Thr Cys Val
195 200 205

Leu Thr Lys Glu Arg Phe Gly Asp Phe Met Leu Phe Gly Ser Leu Ala
210 215 220

Ala Phe Phe Thr Pro Leu Ala Ile Met Ile Val Thr Tyr Phe Leu Thr
225 230 235 240

Ile His Ala Leu Gln Lys Lys Ala Tyr Leu Val Lys Asn Lys Pro Pro
245 250 255

Gln Arg Leu Thr Trp Leu Thr Val Ser Thr Val Phe Gln Arg Asp Glu
260 265 270

Thr Pro Cys Ser Ser Pro Glu Lys Val Ala Met Leu Asp Gly Ser Arg
275 280 285

Lys Asp Lys Ala Leu Pro Asn Ser Gly Asp Glu Thr Leu Met Arg Arg
290 295 300

Thr Ser Thr Ile Gly Lys Lys Ser Val Gln Thr Ile Ser Asn Glu Gln
305 310 315 320

Arg Ala Ser Lys Val Leu Gly Ile Val Phe Phe Leu Phe Leu Leu Met
325 330 335

Trp Cys Pro Phe Phe Ile Thr Asn Ile Thr Leu Val Leu Cys Asp Ser
340 345 350

Cys Asn Gln Thr Thr Leu Gln Met Leu Leu Glu Ile Phe Val Trp Ile
355 360 365

Gly Tyr Val Ser Ser Gly Val Asn Pro Leu Val Tyr Thr Leu Phe Asn
370 375 380

Lys Thr Phe Arg Asp Ala Phe Gly Arg Tyr Ile Thr Cys Asn Tyr Arg
385 390 395 400

Ala Thr Lys Ser Val Lys Thr Leu Arg Lys Arg Ser Ser Lys Ile Tyr
405 410 415

Phe Arg Asn Pro Met Ala Glu Asn Ser Lys Phe Phe Lys Lys His Gly
420 425 430

Ile Arg Asn Gly Ile Asn Pro Ala Met Tyr Gln Ser Pro Met Arg Leu
435 440 445

Arg Ser Ser Thr Ile Gln Ser Ser Ser Ile Ile Leu Leu Asp Thr Leu
450 455 460

Leu Leu Thr Glu Asn Glu Gly Asp Lys Thr Glu Glu Gln Val Ser Tyr
465 470 475 480

Val

<210> 73
<211> 189
<212> PRT
<213> Homo sapiens

<400> 73

Met Ala Leu Ser Phe Ser Leu Leu Met Ala Val Leu Val Leu Ser Tyr
1 5 10 15

Lys Ser Ile Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Ser Leu
20 25 30

Gly Asn Arg Arg Ala Leu Ile Leu Leu Ala Gln Met Gly Arg Ile Ser
35 40 45

Pro Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe Pro Gln Glu
50 55 60

Glu Phe Asp Gly Asn Gln Phe Gln Lys Ala Gln Ala Ile Ser Val Leu
65 70 75 80

His Glu Met Ile Gln Gln Thr Phe Asn Leu Phe Ser Thr Lys Asp Ser
85 90 95

Ser Ala Thr Trp Glu Gln Ser Leu Leu Glu Lys Phe Ser Thr Glu Leu
100 105 110

Asn Gln Gln Leu Asn Asp Met Glu Ala Cys Val Ile Gln Glu Val Gly
115 120 125

Val Glu Glu Thr Pro Leu Met Asn Val Asp Ser Ile Leu Ala Val Lys
130 135 140

Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Thr Glu Lys Lys Tyr Ser
145 150 155 160

Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser
165 170 175

Leu Ser Lys Ile Phe Gln Glu Arg Leu Arg Arg Lys Glu
180 185

<210> 74
<211> 153
<212> PRT
<213> Homo sapiens

<400> 74

Met Gly Lys Ile Ser Ser Leu Pro Thr Gln Leu Phe Lys Cys Cys Phe
1 5 10 15

Cys Asp Phe Leu Lys Val Lys Met His Thr Met Ser Ser Ser His Leu
20 25 30

Phe Tyr Leu Ala Leu Cys Leu Leu Thr Phe Thr Ser Ser Ala Thr Ala
35 40 45

Gly Pro Glu Thr Leu Cys Gly Ala Glu Leu Val Asp Ala Leu Gln Phe
50 55 60

Val Cys Gly Asp Arg Gly Phe Tyr Phe Asn Lys Pro Thr Gly Tyr Gly
65 70 75 80

Ser Ser Ser Arg Arg Ala Pro Gln Thr Gly Ile Val Asp Glu Cys Cys
85 90 95

Phe Arg Ser Cys Asp Leu Arg Arg Leu Glu Met Tyr Cys Ala Pro Leu
100 105 110

Lys Pro Ala Lys Ser Ala Arg Ser Val Arg Ala Gln Arg His Thr Asp
115 120 125

Met Pro Lys Thr Gln Lys Glu Val His Leu Lys Asn Ala Ser Arg Gly
130 135 140

Ser Ala Gly Asn Lys Asn Tyr Arg Met
145 150

<210> 75
<211> 632
<212> PRT
<213> Homo sapiens

<220>
<221> UNSURE
<222> (199)..(199)
<223> Xaa = any amino acid

<400> 75

Met Glu Thr Pro Ala Ala Ala Ala Pro Ala Gly Ser Leu Phe Pro Ser
1 5 10 15

Phe Leu Leu Leu Ala Cys Gly Thr Leu Val Ala Ala Leu Leu Gly Ala
20 25 30

Ala His Arg Leu Gly Leu Phe Tyr Gln Leu Leu His Lys Val Asp Lys
35 40 45

Ala Ser Val Arg His Gly Gly Glu Asn Val Ala Ala Val Leu Arg Ala
50 55 60

His Gly Val Arg Phe Ile Phe Thr Leu Val Gly Gly His Ile Ser Pro
65 70 75 80

Leu Leu Val Ala Cys Glu Lys Leu Gly Ile Arg Val Val Asp Thr Arg
85 90 95

His Glu Val Thr Ala Val Phe Ala Ala Asp Ala Met Ala Arg Leu Ser
100 105 110

Gly Thr Val Gly Val Ala Ala Val Thr Ala Gly Pro Gly Leu Thr Asn
115 120 125

Thr Val Thr Ala Val Lys Asn Ala Gln Met Ala Gln Ser Pro Ile Leu
130 135 140

Leu Leu Gly Gly Ala Ala Ser Thr Leu Leu Gln Asn Arg Gly Ala Leu
145 150 155 160

Gln Ala Val Asp Gln Leu Ser Leu Phe Arg Pro Leu Cys Lys Phe Cys
165 170 175

Val Ser Val Arg Arg Val Arg Asp Ile Val Pro Thr Leu Arg Ala Ala
180 185 190

Met Ala Ala Ala Gln Ser Xaa Thr Pro Gly Pro Val Phe Val Glu Leu
195 200 205

Pro Val Asp Val Leu Tyr Pro Tyr Phe Met Val Gln Lys Glu Met Val
210 215 220

Pro Ala Lys Pro Pro Lys Gly Leu Val Gly Arg Val Val Ser Trp Tyr
225 230 235 240

Leu Glu Asn Tyr Leu Ala Asn Leu Phe Ala Gly Ala Trp Glu Pro Gln
245 250 255

Pro Glu Gly Pro Leu Pro Leu Asp Ile Pro Gln Ala Ser Pro Gln Gln
260 265 270

Val Gln Arg Cys Val Glu Ile Leu Ser Arg Ala Lys Arg Pro Leu Met
275 280 285

Val Leu Gly Ser Gln Ala Leu Leu Thr Pro Thr Ser Ala Asp Lys Leu
290 295 300

Arg Ala Ala Val Glu Thr Leu Gly Val Pro Cys Phe Leu Gly Gly Met
305 310 315 320

Ala Arg Gly Leu Leu Gly Arg Asn His Pro Leu His Ile Arg Glu Asn
325 330 335

Arg Ser Ala Ala Leu Lys Lys Ala Asp Val Ile Val Leu Ala Gly Thr
340 345 350

Val Cys Asp Phe Arg Leu Ser Tyr Gly Arg Val Leu Ser His Ser Ser
355 360 365

Lys Ile Ile Ile Val Asn Arg Asn Arg Glu Glu Met Leu Leu Asn Ser
370 375 380

Asp Ile Phe Trp Lys Pro Gln Glu Ala Val Gln Gly Asp Val Gly Ser
385 390 395 400

Phe Val Leu Lys Leu Val Glu Gly Leu Gln Gly Gln Thr Trp Ala Pro
405 410 415

Asp Trp Val Glu Glu Leu Arg Glu Ala Asp Arg Gln Lys Glu Gln Thr
420 425 430

Phe Arg Glu Lys Ala Ala Met Pro Val Ala Gln His Leu Asn Pro Val
435 440 445

Gln Val Leu Gln Leu Val Glu Glu Thr Leu Pro Asp Asn Ser Ile Leu
450 455 460

Val Val Asp Gly Gly Asp Phe Val Gly Thr Ala Ala His Leu Val Gln
465 470 475 480

Pro Arg Gly Pro Leu Arg Trp Leu Asp Pro Gly Ala Phe Gly Thr Leu
485 490 495

Gly Val Gly Ala Gly Phe Ala Leu Gly Ala Lys Leu Cys Arg Pro Asp
500 505 510

Ala Glu Val Trp Cys Leu Phe Gly Asp Gly Ala Phe Gly Tyr Ser Leu
515 520 525

Ile Glu Phe Asp Thr Phe Val Arg His Lys Ile Pro Val Met Ala Leu
530 535 540

Val Gly Asn Asp Ala Gly Trp Thr Gln Ile Ser Arg Glu Gln Val Pro
545 550 555 560

Ser Leu Gly Ser Asn Val Ala Cys Gly Leu Ala Tyr Thr Asp Tyr His
565 570 575

Lys Ala Ala Met Gly Leu Gly Ala Arg Gly Leu Leu Leu Ser Arg Glu
580 585 590

Asn Glu Asp Gln Val Val Lys Val Leu His Asp Ala Gln Gln Gln Cys
595 600 605

Arg Asp Gly His Pro Val Val Val Asn Ile Leu Ile Gly Arg Thr Asp
610 615 620

Phe Arg Asp Gly Ser Ile Ala Val
625 630

<210> 76
<211> 349
<212> PRT

<213> Homo sapiens

<400> 76

Met Pro Val Glu Arg Met Arg Met Arg Pro Trp Leu Glu Glu Gln Ile
1 5 10 15

Asn Ser Asn Thr Ile Pro Gly Leu Lys Trp Leu Asn Lys Glu Lys Lys
20 25 30

Ile Phe Gln Ile Pro Trp Met His Ala Ala Arg His Gly Trp Asp Val
35 40 45

Glu Lys Asp Ala Pro Leu Phe Arg Asn Arg Ala Ile His Thr Gly Lys
50 55 60

His Gln Pro Gly Val Asp Lys Pro Asp Pro Lys Thr Trp Lys Ala Asn
65 70 75 80

Phe Arg Cys Ala Met Asn Ser Leu Pro Asp Ile Glu Glu Val Lys Asp
85 90 95

Lys Ser Ile Lys Lys Gly Asn Asn Ala Phe Arg Val Tyr Arg Met Leu
100 105 110

Pro Leu Ser Glu Arg Pro Ser Lys Lys Gly Lys Lys Pro Lys Thr Glu
115 120 125

Lys Glu Asp Lys Val Lys His Ile Lys Gln Glu Pro Val Glu Ser Ser
130 135 140

Leu Gly Leu Ser Asn Gly Val Ser Asp Leu Ser Pro Glu Tyr Ala Val
145 150 155 160

Leu Thr Ser Thr Ile Lys Asn Glu Val Asp Ser Thr Val Asn Ile Ile
165 170 175

Val Val Gly Gln Ser His Leu Asp Ser Asn Ile Glu Asn Gln Glu Ile
180 185 190

Val Thr Asn Pro Pro Asp Ile Cys Gln Val Val Glu Val Thr Thr Glu
195 200 205

Ser Asp Glu Gln Pro Val Ser Met Ser Glu Leu Tyr Pro Leu Gln Ile
210 215 220

Ser Pro Val Ser Ser Tyr Ala Glu Ser Glu Thr Thr Asp Ser Val Pro
225 230 235 240

Ser Asp Glu Glu Ser Ala Glu Gly Arg Pro His Trp Arg Lys Arg Asn
245 250 255

Ile Glu Gly Lys Gln Tyr Leu Ser Asn Met Gly Thr Arg Gly Ser Tyr
260 265 270

Leu Leu Pro Gly Met Ala Ser Phe Val Thr Ser Asn Lys Pro Asp Leu
275 280 285

Gln Val Thr Ile Lys Glu Glu Ser Asn Pro Val Pro Tyr Asn Ser Ser
290 295 300

Trp Pro Pro Phe Gln Asp Leu Pro Leu Ser Ser Ser Met Thr Pro Ala
305 310 315 320

Ser Ser Ser Ser Arg Pro Asp Arg Glu Thr Arg Ala Ser Val Ile Lys
325 330 335

Lys Thr Ser Asp Ile Thr Gln Ala Arg Val Lys Ser Cys
340 345

<210> 77
<211> 338
<212> PRT
<213> Homo sapiens

<400> 77

Met Ile Asn Ser Thr Ser Thr Gln Pro Pro Asp Glu Ser Cys Ser Gln
1 5 10 15

Asn Leu Leu Ile Thr Gln Gln Ile Ile Pro Val Leu Tyr Cys Met Val
20 25 30

Phe Ile Ala Gly Ile Leu Leu Asn Gly Val Ser Gly Trp Ile Phe Phe
35 40 45

Tyr Val Pro Ser Ser Lys Ser Phe Ile Ile Tyr Leu Lys Asn Ile Val
50 55 60

Ile Ala Asp Phe Val Met Ser Leu Thr Phe Pro Phe Lys Ile Leu Gly
65 70 75 80

Asp Ser Gly Leu Gly Pro Trp Gln Leu Asn Val Phe Val Cys Arg Val
85 90 95

Ser Ala Val Leu Phe Tyr Val Asn Met Tyr Val Ser Ile Val Phe Phe
100 105 110

Gly Leu Ile Ser Phe Asp Arg Tyr Tyr Lys Ile Val Lys Pro Leu Trp
115 120 125

Thr Ser Phe Ile Gln Ser Val Ser Tyr Ser Lys Leu Leu Ser Val Ile
130 135 140

Val Trp Met Leu Met Leu Leu Leu Ala Val Pro Asn Ile Ile Leu Thr
145 150 155 160

Asn Gln Ser Val Arg Glu Val Thr Gln Ile Lys Cys Ile Glu Leu Lys
165 170 175

Ser Glu Leu Gly Arg Lys Trp His Lys Ala Ser Asn Tyr Ile Phe Val
180 185 190

Ala Ile Phe Trp Ile Val Phe Leu Leu Leu Ile Val Phe Tyr Thr Ala
195 200 205

Ile Thr Lys Lys Ile Phe Lys Ser His Leu Lys Ser Ser Arg Asn Ser
210 215 220

Thr Ser Val Lys Lys Lys Ser Ser Arg Asn Ile Phe Ser Ile Val Phe

225 230 235 240

Val Phe Phe Val Cys Phe Val Pro Tyr His Ile Ala Arg Ile Pro Tyr
245 250 255

Thr Lys Ser Gln Thr Glu Ala His Tyr Ser Cys Gln Ser Lys Glu Ile
260 265 270

Leu Arg Tyr Met Lys Glu Phe Thr Leu Leu Leu Ser Ala Ala Asn Val
275 280 285

Cys Leu Asp Pro Ile Ile Tyr Phe Phe Leu Cys Gln Pro Phe Arg Glu
290 295 300

Ile Leu Cys Lys Lys Leu His Ile Pro Leu Lys Ala Gln Asn Asp Leu
305 310 315 320

Asp Ile Ser Arg Ile Lys Arg Gly Asn Thr Thr Leu Glu Ser Thr Asp
325 330 335

Thr Leu

<210> 78
<211> 232
<212> PRT
<213> Homo sapiens

<400> 78

Leu Glu Thr Gln Ile Glu Ala Leu Lys Glu Glu Leu Leu Phe Met Lys
1 5 10 15

Lys Asn His Glu Glu Glu Val Lys Gly Leu Gln Ala Gln Ile Ala Ser
20 25 30

Ser Gly Leu Thr Val Glu Val Asp Ala Pro Lys Ser Gln Asp Leu Ser
35 40 45

Lys Ile Met Ala Asp Ile Arg Ala Gln Tyr Asp Glu Leu Ala Arg Lys
50 55 60

Asn Arg Glu Glu Leu Asp Lys Tyr Trp Ser Gln Gln Ile Glu Glu Ser
65 70 75 80

Thr Thr Val Val Thr Thr Gln Ser Ala Glu Val Gly Ala Ala Glu Thr
85 90 95

Thr Leu Thr Glu Leu Arg Arg Thr Val Gln Ser Leu Glu Ile Arg Leu
100 105 110

Asp Arg Met Arg Asn Leu Lys Ala Ser Leu Glu Asn Ser Leu Arg Glu
115 120 125

Val Glu Ala Arg Tyr Ala Leu Gln Met Glu Gln Leu Asn Gly Ile Leu
130 135 140

Leu His Leu Glu Ser Glu Leu Ala Gln Thr Arg Ala Glu Gly Gln Arg
145 150 155 160

Gln Ala Gln Glu Tyr Glu Ala Leu Leu Asn Ile Lys Val Lys Leu Glu
165 170 175

Ala Glu Ile Ala Thr Tyr Arg Arg Leu Leu Glu Asp Gly Glu Asp Phe
180 185 190

Asn Leu Gly Asp Ala Leu Asp Ser Ser Asn Ser Met Gln Thr Ile Gln
195 200 205

Lys Thr Thr Thr Arg Arg Ile Val Asp Gly Lys Val Val Ser Glu Thr
210 215 220

Asn Asp Thr Lys Val Leu Arg His
225 230

<210> 79
<211> 483
<212> PRT
<213> Homo sapiens

<400> 79

Met Ser Ile Arg Val Thr Gln Lys Ser Tyr Lys Val Ser Thr Ser Gly
1 5 10 15

Pro Arg Ala Phe Ser Ser Arg Ser Tyr Thr Ser Gly Pro Gly Ser Arg
20 25 30

Ile Ser Ser Ser Ser Phe Ser Arg Val Gly Ser Ser Asn Phe Arg Gly
35 40 45

Gly Leu Gly Gly Gly Tyr Gly Gly Ala Ser Gly Met Gly Gly Ile Thr
50 55 60

Ala Val Thr Val Asn Gln Ser Leu Leu Ser Pro Leu Val Leu Glu Val
65 70 75 80

Asp Pro Asn Ile Gln Ala Val Arg Thr Gln Glu Lys Glu Gln Ile Lys
85 90 95

Thr Leu Asn Asn Lys Phe Ala Ser Phe Ile Asp Lys Val Arg Phe Leu
100 105 110

Glu Gln Gln Asn Lys Met Leu Glu Thr Lys Trp Ser Leu Leu Gln Gln
115 120 125

Gln Lys Thr Ala Arg Ser Asn Met Asp Asn Met Phe Glu Ser Tyr Ile
130 135 140

Asn Asn Leu Arg Arg Gln Leu Glu Thr Leu Gly Gln Glu Lys Leu Lys
145 150 155 160

Leu Glu Ala Glu Leu Gly Asn Met Gln Gly Leu Val Glu Asp Phe Lys
165 170 175

Asn Lys Tyr Glu Asp Glu Ile Asn Lys Arg Thr Glu Met Glu Asn Glu
180 185 190

Phe Val Leu Ile Lys Lys Asp Val Asp Glu Ala Tyr Met Asn Lys Val
195 200 205

Glu Leu Glu Ser Arg Leu Glu Gly Leu Thr Asp Glu Ile Asn Phe Leu
210 215 220

Arg Gln Leu Tyr Glu Glu Glu Ile Arg Glu Leu Gln Ser Gln Ile Ser
225 230 235 240

Asp Thr Ser Val Val Leu Ser Met Asp Asn Ser Arg Ser Leu Asp Met
245 250 255

Asp Ser Ile Ile Ala Glu Val Lys Ala Gln Tyr Glu Asp Ile Ala Asn
260 265 270

Arg Ser Arg Ala Glu Ala Glu Ser Met Tyr Gln Ile Lys Tyr Glu Glu
275 280 285

Leu Gln Ser Leu Ala Gly Lys His Gly Asp Asp Leu Arg Arg Thr Lys
290 295 300

Thr Glu Ile Ser Glu Met Asn Arg Asn Ile Ser Arg Leu Gln Ala Glu
305 310 315 320

Ile Glu Gly Leu Lys Gly Gln Arg Ala Ser Leu Glu Ala Ala Ile Ala
325 330 335

Asp Ala Glu Gln Arg Gly Glu Leu Ala Ile Lys Asp Ala Asn Ala Lys
340 345 350

Leu Ser Glu Leu Glu Ala Ala Leu Gln Arg Ala Lys Gln Asp Met Ala
355 360 365

Arg Gln Leu Arg Glu Tyr Gln Glu Leu Met Asn Val Lys Leu Ala Leu
370 375 380

Asp Ile Glu Ile Ala Thr Tyr Arg Lys Leu Leu Glu Gly Glu Glu Ser
385 390 395 400

Arg Leu Glu Ser Gly Met Gln Asn Met Ser Ile His Thr Lys Thr Thr
405 410 415

Ser Gly Tyr Ala Gly Gly Leu Ser Ser Ala Tyr Gly Gly Leu Thr Ser
420 425 430

Pro Gly Leu Ser Tyr Ser Leu Gly Ser Ser Phe Gly Ser Gly Ala Gly
435 440 445

Ser Ser Ser Phe Ser Arg Thr Ser Ser Ser Arg Ala Val Val Val Lys
450 455 460

Lys Ile Glu Thr Arg Asp Gly Lys Leu Val Ser Glu Ser Ser Asp Val
465 470 475 480

Leu Pro Lys

<210> 80
<211> 440
<212> PRT
<213> Homo sapiens

<400> 80

Met Gly Pro Pro Gly Ser Pro Trp Gln Trp Val Thr Leu Leu Leu Gly
1 5 10 15

Leu Leu Leu Pro Pro Ala Ala Pro Phe Trp Leu Leu Asn Val Leu Phe
20 25 30

Pro Pro His Thr Thr Pro Lys Ala Glu Leu Ser Asn His Thr Arg Pro
35 40 45

Val Ile Leu Val Pro Gly Cys Leu Gly Asn Gln Leu Glu Ala Lys Leu
50 55 60

Asp Lys Pro Asp Val Val Asn Trp Met Cys Tyr Arg Lys Thr Glu Asp
65 70 75 80

Phe Phe Thr Ile Trp Leu Asp Leu Asn Met Phe Leu Pro Leu Gly Val
85 90 95

Asp Cys Trp Ile Asp Asn Thr Arg Val Val Tyr Asn Arg Ser Ser Gly
100 105 110

Leu Val Ser Asn Ala Pro Gly Val Gln Ile Arg Val Pro Gly Phe Gly
115 120 125

Lys Thr Tyr Ser Val Glu Tyr Leu Asp Ser Ser Lys Leu Ala Gly Tyr
130 135 140

Leu His Thr Leu Val Gln Asn Leu Val Asn Asn Gly Tyr Val Arg Asp
145 150 155 160

Glu Thr Val Arg Ala Ala Pro Tyr Asp Trp Arg Leu Glu Pro Gly Gln
165 170 175

Gln Glu Glu Tyr Tyr Arg Lys Leu Ala Gly Leu Val Glu Glu Met His
180 185 190

Ala Ala Tyr Gly Lys Pro Val Phe Leu Ile Gly His Ser Leu Gly Cys
195 200 205

Leu His Leu Leu Tyr Phe Leu Leu Arg Gln Pro Gln Ala Trp Lys Asp
210 215 220

Arg Phe Ile Asp Gly Phe Ile Ser Leu Gly Ala Pro Trp Gly Gly Ser
225 230 235 240

Ile Lys Pro Met Leu Val Leu Ala Ser Gly Asp Asn Gln Gly Ile Pro
245 250 255

Ile Met Ser Ser Ile Lys Leu Lys Glu Glu Gln Arg Ile Thr Thr Thr
260 265 270

Ser Pro Trp Met Phe Pro Ser Arg Met Ala Trp Pro Glu Asp His Val
275 280 285

Phe Ile Ser Thr Pro Ser Phe Asn Tyr Thr Gly Arg Asp Phe Gln Arg
290 295 300

Phe Phe Ala Asp Leu His Phe Glu Glu Gly Trp Tyr Met Trp Leu Gln

305 310 315 320

Ser Arg Asp Leu Leu Ala Gly Leu Pro Ala Pro Gly Val Glu Val Tyr
325 330 335

Cys Leu Tyr Gly Val Gly Leu Pro Thr Pro Arg Thr Tyr Ile Tyr Asp
340 345 350

His Gly Phe Pro Tyr Thr Asp Pro Val Gly Val Leu Tyr Glu Asp Gly
355 360 365

Asp Asp Thr Val Ala Thr Arg Ser Thr Glu Leu Cys Gly Leu Trp Gln
370 375 380

Gly Arg Gln Pro Gln Pro Val His Leu Leu Pro Leu His Gly Ile Gln
385 390 395 400

His Leu Asn Met Val Phe Ser Asn Leu Thr Leu Glu His Ile Asn Ala
405 410 415

Ile Leu Leu Gly Ala Tyr Arg Gln Gly Pro Pro Ala Ser Pro Thr Ala
420 425 430

Ser Pro Glu Pro Pro Pro Pro Glu
435 440

<210> 81
<211> 135
<212> PRT
<213> Homo sapiens

<400> 81

Met Ala Cys Gly Leu Val Ala Ser Asn Leu Asn Leu Lys Pro Gly Glu
1 5 10 15

Cys Leu Arg Val Arg Gly Glu Val Ala Pro Asp Ala Lys Ser Phe Val
20 25 30

Leu Asn Leu Gly Lys Asp Ser Asn Asn Leu Cys Leu His Phe Asn Pro
35 40 45

Arg Phe Asn Ala His Gly Asp Ala Asn Thr Ile Val Cys Asn Ser Lys
50 55 60

Asp Gly Gly Ala Trp Gly Thr Glu Gln Arg Glu Ala Val Phe Pro Phe
65 70 75 80

Gln Pro Gly Ser Val Ala Glu Val Cys Ile Thr Phe Asp Gln Ala Asn
85 90 95

Leu Thr Val Lys Leu Pro Asp Gly Tyr Glu Phe Lys Phe Pro Asn Arg
100 105 110

Leu Asn Leu Glu Ala Ile Asn Tyr Met Ala Ala Asp Gly Asp Phe Lys
115 120 125

Ile Lys Cys Val Ala Phe Asp
130 135

<210> 82
<211> 314
<212> PRT
<213> Homo sapiens

<400> 82

Met Ala Pro Pro Gln Val Leu Ala Phe Gly Leu Leu Leu Ala Ala Ala
1 5 10 15

Thr Ala Thr Phe Ala Ala Ala Gln Glu Glu Cys Val Cys Glu Asn Tyr
20 25 30

Lys Leu Ala Val Asn Cys Phe Val Asn Asn Asn Arg Gln Cys Gln Cys
35 40 45

Thr Ser Val Gly Ala Gln Asn Thr Val Ile Cys Ser Lys Leu Ala Ala
50 55 60

Lys Cys Leu Val Met Lys Ala Glu Met Asn Gly Ser Lys Leu Gly Arg
65 70 75 80

Arg Ala Lys Pro Glu Gly Ala Leu Gln Asn Asn Asp Gly Leu Tyr Asp
85 90 95

Pro Asp Cys Asp Glu Ser Gly Leu Phe Lys Ala Lys Gln Cys Asn Gly
100 105 110

Thr Ser Thr Cys Trp Cys Val Asn Thr Ala Gly Val Arg Arg Thr Asp
115 120 125

Lys Asp Thr Glu Ile Thr Cys Ser Glu Arg Val Arg Thr Tyr Trp Ile
130 135 140

Ile Ile Glu Leu Lys His Lys Ala Arg Glu Lys Pro Tyr Asp Ser Lys
145 150 155 160

Ser Leu Arg Thr Ala Leu Gln Lys Glu Ile Thr Thr Arg Tyr Gln Leu
165 170 175

Asp Pro Lys Phe Ile Thr Ser Ile Leu Tyr Glu Asn Asn Val Ile Thr
180 185 190

Ile Asp Leu Val Gln Asn Ser Ser Gln Lys Thr Gln Asn Asp Val Asp
195 200 205

Ile Ala Asp Val Ala Tyr Tyr Phe Glu Lys Asp Val Lys Gly Glu Ser
210 215 220

Leu Phe His Ser Lys Lys Met Asp Leu Thr Val Asn Gly Glu Gln Leu
225 230 235 240

Asp Leu Asp Pro Gly Gln Thr Leu Ile Tyr Tyr Val Asp Glu Lys Ala
245 250 255

Pro Glu Phe Ser Met Gln Gly Leu Lys Ala Gly Val Ile Ala Val Ile
260 265 270

Val Val Val Val Ile Ala Val Val Ala Gly Ile Val Val Leu Val Ile
275 280 285

Ser Arg Lys Lys Arg Met Ala Lys Tyr Glu Lys Ala Glu Ile Lys Glu
290 295 300

Met Gly Glu Met His Arg Glu Leu Asn Ala
305 310

<210> 83
<211> 720
<212> PRT
<213> Homo sapiens

<400> 83

Lys Ser Val Trp Lys Gly Gly Leu Arg Glu Arg Asp Pro Arg Gly Thr
1 5 10 15

Arg Gly Gly Gly Arg Arg Gly Thr Gly Ser Gln Pro Ala Leu Cys Leu
20 25 30

Gly Ala Gly Arg Gln Glu Gly Ala Met Ala Leu Asp Gly Ile Arg Met
35 40 45

Pro Asp Gly Cys Tyr Ala Asp Gly Thr Trp Glu Leu Ser Val His Val
50 55 60

Thr Asp Leu Asn Arg Asp Ile Thr Leu Arg Val Thr Gly Glu Val His
65 70 75 80

Ile Gly Gly Val Met Leu Lys Leu Val Glu Lys Leu Asp Val Lys Lys
85 90 95

Asp Trp Ser Asp His Ala Leu Trp Trp Glu Lys Lys Arg Thr Trp Leu
100 105 110

Leu Lys Thr His Trp Thr Leu Asp Lys Tyr Gly Ile Gln Ala Asp Ala
115 120 125

Lys Leu Gln Phe Thr Pro Gln His Lys Leu Leu Arg Leu Gln Leu Pro
130 135 140

Asn Met Lys Tyr Val Lys Val Lys Val Asn Phe Ser Asp Arg Val Phe
145 150 155 160

Lys Ala Val Ser Asp Ile Cys Lys Thr Phe Asn Ile Arg His Pro Glu
165 170 175

Glu Leu Ser Leu Leu Lys Lys Pro Arg Asp Pro Thr Lys Lys Lys Lys
180 185 190

Lys Lys Leu Asp Asp Gln Ser Glu Asp Glu Ala Leu Glu Leu Glu Gly
195 200 205

Pro Leu Ile Thr Pro Gly Ser Gly Ser Ile Tyr Ser Ser Pro Gly Leu
210 215 220

Tyr Ser Lys Thr Met Thr Pro Thr Tyr Asp Ala His Asp Gly Ser Pro
225 230 235 240

Leu Ser Pro Thr Ser Ala Trp Phe Gly Asp Ser Ala Leu Ser Glu Gly

245 250 255

Asn Pro Gly Ile Leu Ala Val Ser Gln Pro Ile Thr Ser Pro Glu Ile
260 265 270

Leu Ala Lys Met Phe Lys Pro Gln Ala Leu Leu Asp Lys Ala Lys Ile
275 280 285

Asn Gln Gly Trp Leu Asp Ser Ser Arg Ser Leu Met Glu Gln Asp Val
290 295 300

Lys Glu Asn Glu Ala Leu Leu Leu Arg Phe Lys Tyr Tyr Ser Phe Phe
305 310 315 320

Asp Leu Asn Pro Lys Tyr Asp Ala Ile Arg Ile Asn Gln Leu Tyr Glu
325 330 335

Gln Ala Lys Trp Ala Ile Leu Leu Glu Glu Ile Glu Cys Thr Glu Glu
340 345 350

Glu Met Met Met Phe Ala Ala Leu Gln Tyr His Ile Asn Lys Leu Ser
355 360 365

Ile Met Thr Ser Glu Asn His Leu Asn Asn Ser Asp Lys Glu Val Asp
370 375 380

Glu Val Asp Ala Ala Leu Ser Asp Leu Glu Ile Thr Leu Glu Gly Gly
385 390 395 400

Lys Thr Ser Thr Ile Leu Gly Asp Ile Thr Ser Ile Pro Glu Leu Ala
405 410 415

Asp Tyr Ile Lys Val Phe Lys Pro Lys Lys Leu Thr Leu Lys Gly Tyr
420 425 430

Lys Gln Tyr Trp Cys Thr Phe Lys Asp Thr Ser Ile Ser Cys Tyr Lys
435 440 445

Ser Lys Glu Glu Ser Ser Gly Thr Pro Ala His Gln Met Asn Leu Arg
450 455 460

Gly Cys Glu Val Thr Pro Asp Val Asn Ile Ser Gly Gln Lys Phe Asn
465 470 475 480

Ile Lys Leu Leu Ile Pro Val Ala Glu Gly Met Asn Glu Ile Trp Leu
485 490 495

Arg Cys Asp Asn Glu Lys Gln Tyr Ala His Trp Met Ala Ala Cys Arg
500 505 510

Leu Ala Ser Lys Gly Lys Thr Met Ala Asp Ser Ser Tyr Asn Leu Glu
515 520 525

Val Gln Asn Ile Leu Ser Phe Leu Lys Met Gln His Leu Asn Pro Asp
530 535 540

Pro Gln Leu Ile Pro Glu Gln Ile Thr Thr Asp Ile Thr Pro Glu Cys
545 550 555 560

Leu Val Ser Pro Arg Tyr Leu Lys Lys Tyr Lys Asn Lys Gln Ile Thr

565 570 575

Ala Arg Ile Leu Glu Ala His Gln Asn Val Ala Gln Met Ser Leu Ile
580 585 590

Glu Ala Lys Met Arg Phe Ile Gln Ala Trp Gln Ser Leu Pro Glu Phe
595 600 605

Gly Ile Thr His Phe Ile Ala Arg Phe Gln Gly Gly Lys Lys Glu Glu
610 615 620

Leu Ile Gly Ile Ala Tyr Asn Arg Leu Ile Arg Met Asp Ala Ser Thr
625 630 635 640

Gly Asp Ala Ile Lys Thr Trp Arg Phe Ser Asn Met Lys Gln Trp Asn
645 650 655

Val Asn Trp Glu Ile Lys Met Val Thr Val Glu Phe Ala Asp Glu Val
660 665 670

Arg Leu Ser Phe Ile Cys Thr Glu Val Asp Cys Lys Val Val His Glu
675 680 685

Phe Ile Gly Gly Tyr Ile Phe Leu Ser Thr Arg Ala Lys Asp Gln Asn
690 695 700

Glu Ser Leu Asp Glu Glu Met Phe Tyr Lys Leu Thr Ser Gly Trp Val
705 710 715 720

<210> 84
<211> 582
<212> PRT
<213> Homo sapiens

<400> 84

Met Ser Pro Ala Pro Arg Pro Pro Arg Cys Leu Leu Leu Pro Leu Leu
1 5 10 15

Thr Leu Gly Thr Ala Leu Ala Ser Leu Gly Ser Ala Gln Ser Ser Ser
20 25 30

Phe Ser Pro Glu Ala Trp Leu Gln Gln Tyr Gly Tyr Leu Pro Pro Gly
35 40 45

Asp Leu Arg Thr His Thr Gln Arg Ser Pro Gln Ser Leu Ser Ala Ala
50 55 60

Ile Ala Ala Met Gln Lys Phe Tyr Gly Leu Gln Val Thr Gly Lys Ala
65 70 75 80

Asp Ala Asp Thr Met Lys Ala Met Arg Arg Pro Arg Cys Gly Val Pro
85 90 95

Asp Lys Phe Gly Ala Glu Ile Lys Ala Asn Val Arg Arg Lys Arg Tyr
100 105 110

Ala Ile Gln Gly Leu Lys Trp Gln His Asn Glu Ile Thr Phe Cys Ile
115 120 125

Gln Asn Tyr Thr Pro Lys Val Gly Glu Tyr Ala Thr Tyr Glu Ala Ile
130 135 140

Arg Lys Ala Phe Arg Val Trp Glu Ser Ala Thr Pro Leu Arg Phe Arg
145 150 155 160

Glu Val Pro Tyr Ala Tyr Ile Arg Glu Gly His Glu Lys Gln Ala Asp
165 170 175

Ile Met Ile Phe Phe Ala Glu Gly Phe His Gly Asp Ser Thr Pro Phe
180 185 190

Asp Gly Glu Gly Gly Phe Leu Ala His Ala Tyr Phe Pro Gly Pro Asn
195 200 205

Ile Gly Gly Asp Thr His Phe Asp Ser Ala Glu Pro Trp Thr Val Arg
210 215 220

Asn Glu Asp Leu Asn Gly Asn Asp Ile Phe Leu Val Ala Val His Glu
225 230 235 240

Leu Gly His Ala Leu Gly Leu Glu His Ser Ser Asp Pro Ser Ala Ile
245 250 255

Met Ala Pro Phe Tyr Gln Trp Met Asp Thr Glu Asn Phe Val Leu Pro
260 265 270

Asp Asp Asp Arg Arg Gly Ile Gln Gln Leu Tyr Gly Gly Glu Ser Gly
275 280 285

Phe Pro Thr Lys Met Pro Pro Gln Pro Arg Thr Thr Ser Arg Pro Ser
290 295 300

Val Pro Asp Lys Pro Lys Asn Pro Thr Tyr Gly Pro Asn Ile Cys Asp
305 310 315 320

Gly Asn Phe Asp Thr Val Ala Met Leu Arg Gly Glu Met Phe Val Phe
325 330 335

Lys Glu Arg Trp Phe Trp Arg Val Arg Asn Asn Gln Val Met Asp Gly
340 345 350

Tyr Pro Met Pro Ile Gly Gln Phe Trp Arg Gly Leu Pro Ala Ser Ile
355 360 365

Asn Thr Ala Tyr Glu Arg Lys Asp Gly Lys Phe Val Phe Phe Lys Gly
370 375 380

Asp Lys His Trp Val Phe Asp Glu Ala Ser Leu Glu Pro Gly Tyr Pro
385 390 395 400

Lys His Ile Lys Glu Leu Gly Arg Gly Leu Pro Thr Asp Lys Ile Asp
405 410 415

Ala Ala Leu Phe Trp Met Pro Asn Gly Lys Thr Tyr Phe Phe Arg Gly
420 425 430

Asn Lys Tyr Tyr Arg Phe Asn Glu Glu Leu Arg Ala Val Asp Ser Glu
435 440 445

Tyr Pro Lys Asn Ile Lys Val Trp Glu Gly Ile Pro Glu Ser Pro Arg
450 455 460

Gly Ser Phe Met Gly Ser Asp Glu Val Phe Thr Tyr Phe Tyr Lys Gly
465 470 475 480

Asn Lys Tyr Trp Lys Phe Asn Asn Gln Lys Leu Lys Val Glu Pro Gly
485 490 495

Tyr Pro Lys Ser Ala Leu Arg Asp Trp Met Gly Cys Pro Ser Gly Gly
500 505 510

Arg Pro Asp Glu Gly Thr Glu Glu Glu Thr Glu Val Ile Ile Ile Glu
515 520 525

Val Asp Glu Glu Gly Gly Gly Ala Val Ser Ala Ala Ala Val Val Leu
530 535 540

Pro Val Leu Leu Leu Leu Leu Val Leu Ala Val Gly Leu Ala Val Phe
545 550 555 560

Phe Phe Arg Arg His Gly Thr Pro Arg Arg Leu Leu Tyr Cys Gln Arg
565 570 575

Ser Leu Leu Asp Lys Val
580

<210> 85
<211> 1246
<212> PRT
<213> Homo sapiens

<400> 85

Met Leu Ala Ser Ser Ser Arg Ile Arg Ala Ala Trp Thr Arg Ala Leu
1 5 10 15

Leu Leu Pro Leu Leu Leu Ala Gly Pro Val Gly Cys Leu Ser Arg Gln
20 25 30

Glu Leu Phe Pro Phe Gly Pro Gly Gln Gly Asp Leu Glu Leu Glu Asp
35 40 45

Gly Asp Asp Phe Val Ser Pro Ala Leu Glu Leu Ser Gly Ala Leu Arg
50 55 60

Phe Tyr Asp Arg Ser Asp Ile Asp Ala Val Tyr Val Thr Thr Asn Gly
65 70 75 80

Ile Ile Ala Thr Ser Glu Pro Pro Ala Lys Glu Ser His Pro Gly Leu
85 90 95

Phe Pro Pro Thr Phe Gly Ala Val Ala Pro Phe Leu Ala Asp Leu Asp
100 105 110

Thr Thr Asp Gly Leu Gly Lys Val Tyr Tyr Arg Glu Asp Leu Ser Pro
115 120 125

Ser Ile Thr Gln Arg Ala Ala Glu Cys Val His Arg Gly Phe Pro Glu
130 135 140

Ile Ser Phe Gln Pro Ser Ser Ala Val Val Val Thr Trp Glu Ser Val
145 150 155 160

Ala Pro Tyr Gln Gly Pro Ser Arg Asp Pro Asp Gln Lys Gly Lys Arg
165 170 175

Asn Thr Phe Gln Ala Val Leu Ala Ser Ser Asp Ser Ser Ser Tyr Ala
180 185 190

Ile Phe Leu Tyr Pro Glu Asp Gly Leu Gln Phe His Thr Thr Phe Ser
195 200 205

Lys Lys Glu Asn Asn Gln Val Pro Ala Val Val Ala Phe Ser Gln Gly
210 215 220

Ser Val Gly Phe Leu Trp Lys Ser Asn Gly Ala Tyr Asn Ile Phe Ala
225 230 235 240

Asn Asp Arg Glu Ser Ile Glu Asn Leu Ala Lys Ser Ser Asn Ser Gly
245 250 255

Gln Gln Gly Val Trp Val Phe Glu Ile Gly Ser Pro Ala Thr Thr Asn
260 265 270

Gly Val Val Pro Ala Asp Val Ile Leu Gly Thr Glu Asp Gly Ala Glu
275 280 285

Tyr Asp Asp Glu Asp Glu Asp Tyr Asp Leu Ala Thr Thr Arg Leu Gly
290 295 300

Leu Glu Asp Val Gly Thr Thr Pro Phe Ser Tyr Lys Ala Leu Arg Arg
305 310 315 320

Gly Gly Ala Asp Thr Tyr Ser Val Pro Ser Val Leu Ser Pro Arg Arg
325 330 335

Ala Ala Thr Glu Arg Pro Leu Gly Pro Pro Thr Glu Arg Thr Arg Ser
340 345 350

Phe Gln Leu Ala Val Glu Thr Phe His Gln Gln His Pro Gln Val Ile
355 360 365

Asp Val Asp Glu Val Glu Glu Thr Gly Val Val Phe Ser Tyr Asn Thr
370 375 380

Asp Ser Arg Gln Thr Cys Ala Asn Asn Arg His Gln Cys Ser Val His
385 390 395 400

Ala Glu Cys Arg Asp Tyr Ala Thr Gly Phe Cys Cys Ser Cys Val Ala
405 410 415

Gly Tyr Thr Gly Asn Gly Arg Gln Cys Val Ala Glu Gly Ser Pro Gln
420 425 430

Arg Val Asn Gly Lys Val Lys Gly Arg Ile Phe Val Gly Ser Ser Gln
435 440 445

Val Pro Ile Val Phe Glu Asn Thr Asp Leu His Ser Tyr Val Val Met
450 455 460

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Asn His Gly Arg Ser Tyr Thr Ala Ile Ser Thr Ile Pro Glu Thr Val
465                 470                 475                 480

Gly Tyr Ser Leu Leu Pro Leu Ala Pro Val Gly Gly Ile Ile Gly Trp
                485                 490                 495

Met Phe Ala Val Glu Gln Asp Gly Phe Lys Asn Gly Phe Ser Ile Thr
            500                 505                 510

Gly Gly Glu Phe Thr Arg Gln Ala Glu Val Thr Phe Val Gly His Pro
        515                 520                 525

Gly Asn Leu Val Ile Lys Gln Arg Phe Ser Gly Ile Asp Glu His Gly
    530                 535                 540

His Leu Thr Ile Asp Thr Glu Leu Glu Gly Arg Val Pro Gln Ile Pro
545                 550                 555                 560

Phe Gly Ser Ser Val His Ile Glu Pro Tyr Thr Glu Leu Tyr His Tyr
                565                 570                 575

Ser Thr Ser Val Ile Thr Ser Ser Ser Thr Arg Glu Tyr Thr Val Thr
            580                 585                 590

Glu Pro Glu Arg Asp Gly Ala Ser Pro Ser Arg Ile Tyr Thr Tyr Gln
        595                 600                 605

Trp Arg Gln Thr Ile Thr Phe Gln Glu Cys Val His Asp Asp Ser Arg
    610                 615                 620

Pro Ala Leu Pro Ser Thr Gln Gln Leu Ser Val Asp Ser Val Phe Val
625                 630                 635                 640

Leu Tyr Asn Gln Glu Glu Lys Ile Leu Arg Tyr Ala Phe Ser Asn Ser
                645                 650                 655

Ile Gly Pro Val Arg Glu Gly Ser Pro Asp Ala Leu Gln Asn Pro Cys
            660                 665                 670

Tyr Ile Gly Thr His Gly Cys Asp Thr Asn Ala Ala Cys Arg Pro Gly
        675                 680                 685

Pro Arg Thr Gln Phe Thr Cys Glu Cys Ser Ile Gly Phe Arg Gly Asp
    690                 695                 700

Gly Arg Thr Cys Tyr Asp Ile Asp Glu Cys Ser Glu Gln Pro Ser Val
705                 710                 715                 720

Cys Gly Ser His Thr Ile Cys Asn Asn His Pro Gly Thr Phe Arg Cys
                725                 730                 735

Glu Cys Val Glu Gly Tyr Gln Phe Ser Asp Glu Gly Thr Cys Val Ala
            740                 745                 750

Val Val Asp Gln Arg Pro Ile Asn Tyr Cys Glu Thr Gly Leu His Asn
        755                 760                 765

Cys Asp Ile Pro Gln Arg Ala Gln Cys Ile Tyr Thr Gly Gly Ser Ser
    770                 775                 780
```

Tyr Thr Cys Ser Cys Leu Pro Gly Phe Ser Gly Asp Gly Gln Ala Cys
785 790 795 800

Gln Asp Val Asp Glu Cys Gln Pro Ser Arg Cys His Pro Asp Ala Phe
805 810 815

Cys Tyr Asn Thr Pro Gly Ser Phe Thr Cys Gln Cys Lys Pro Gly Tyr
820 825 830

Gln Gly Asp Gly Phe Arg Cys Val Pro Gly Glu Val Glu Lys Thr Arg
835 840 845

Cys Gln His Glu Arg Glu His Ile Leu Gly Ala Ala Gly Ala Thr Asp
850 855 860

Pro Gln Arg Pro Ile Pro Pro Gly Leu Phe Val Pro Glu Cys Asp Ala
865 870 875 880

His Gly His Tyr Ala Pro Thr Gln Cys His Gly Ser Thr Gly Tyr Cys
885 890 895

Trp Cys Val Asp Arg Asp Gly Arg Glu Val Glu Gly Thr Arg Thr Arg
900 905 910

Pro Gly Met Thr Pro Pro Cys Leu Ser Thr Val Ala Pro Pro Ile His
915 920 925

Gln Gly Pro Ala Val Pro Thr Ala Val Ile Pro Leu Pro Pro Gly Thr
930 935 940

His Leu Leu Phe Ala Gln Thr Gly Lys Ile Glu Arg Leu Pro Leu Glu
945 950 955 960

Gly Asn Thr Met Arg Lys Thr Glu Ala Lys Ala Phe Leu His Val Pro
965 970 975

Ala Lys Val Ile Ile Gly Leu Ala Phe Asp Cys Val Asp Lys Met Val
980 985 990

Tyr Trp Thr Asp Ile Thr Glu Pro Ser Ile Gly Arg Ala Ser Leu His
995 1000 1005

Gly Gly Glu Pro Thr Thr Ile Ile Arg Gln Asp Leu Gly Ser Pro
1010 1015 1020

Glu Gly Ile Ala Val Asp His Leu Gly Arg Asn Ile Phe Trp Thr
1025 1030 1035

Asp Ser Asn Leu Asp Arg Ile Glu Val Ala Lys Leu Asp Gly Thr
1040 1045 1050

Gln Arg Arg Val Leu Phe Glu Thr Asp Leu Val Asn Pro Arg Gly
1055 1060 1065

Ile Val Thr Asp Ser Val Arg Gly Asn Leu Tyr Trp Thr Asp Trp
1070 1075 1080

Asn Arg Asp Asn Pro Lys Ile Glu Thr Ser Tyr Met Asp Gly Thr
1085 1090 1095

Asn Arg Arg Ile Leu Val Gln Asp Asp Leu Gly Leu Pro Asn Gly
1100 1105 1110

Leu His Phe Asp Ala Phe Ser Ser Gln Leu Cys Trp Val Asp Ala
1115 1120 1125

Gly Thr Asn Arg Ala Glu Cys Leu Asn Pro Ser Gln Pro Ser Arg
1130 1135 1140

Arg Lys Ala Leu Glu Gly Leu Gln Tyr Pro Phe Ala Val Thr Ser
1145 1150 1155

Tyr Gly Lys Asn Leu Tyr Phe Thr Asp Trp Lys Met Asn Ser Val
1160 1165 1170

Val Ala Leu Asp Leu Ala Ile Ser Lys Glu Thr Asp Ala Phe Gln
1175 1180 1185

Pro His Lys Gln Thr Arg Leu Tyr Gly Ile Thr Thr Ala Leu Ser
1190 1195 1200

Gln Cys Pro Gln Gly His Asn Tyr Cys Ser Val Asn Asn Gly Gly
1205 1210 1215

Cys Thr His Leu Cys Leu Ala Thr Pro Gly Ser Arg Thr Cys Arg
1220 1225 1230

Cys Pro Asp Asn Thr Leu Gly Val Asp Cys Ile Glu Arg
1235 1240 1245

<210> 86
<211> 423
<212> PRT
<213> Homo sapiens

<400> 86

Met Ala Met Val Val Ser Ser Trp Arg Asp Pro Gln Asp Asp Val Ala
1 5 10 15

Gly Gly Asn Pro Gly Gly Pro Asn Pro Ala Ala Gln Ala Ala Arg Gly
20 25 30

Gly Gly Gly Gly Ala Gly Glu Gln Gln Gln Gln Ala Gly Ser Gly Ala
35 40 45

Pro His Thr Pro Gln Thr Pro Gly Gln Pro Gly Ala Pro Ala Thr Pro
50 55 60

Gly Thr Ala Gly Asp Lys Gly Gln Gly Pro Pro Gly Ser Gly Gln Ser
65 70 75 80

Gln Gln His Ile Glu Cys Val Val Cys Gly Asp Lys Ser Ser Gly Lys
85 90 95

His Tyr Gly Gln Phe Thr Cys Glu Gly Cys Lys Ser Phe Phe Lys Arg
100 105 110

Ser Val Arg Arg Asn Leu Thr Tyr Thr Cys Arg Ala Asn Arg Asn Cys

```
        115                 120                 125

Pro Ile Asp Gln His His Arg Asn Gln Cys Gln Tyr Cys Arg Leu Lys
    130                 135                 140

Lys Cys Leu Lys Val Gly Met Arg Arg Glu Ala Val Gln Arg Gly Arg
145                 150                 155                 160

Met Pro Pro Thr Gln Pro Asn Pro Gly Gln Tyr Ala Leu Thr Asn Gly
                165                 170                 175

Asp Pro Leu Asn Gly His Cys Tyr Leu Ser Gly Tyr Ile Ser Leu Leu
            180                 185                 190

Leu Arg Ala Glu Pro Tyr Pro Thr Ser Arg Tyr Gly Ser Gln Cys Met
        195                 200                 205

Gln Pro Asn Asn Ile Met Gly Ile Glu Asn Ile Cys Glu Leu Ala Ala
    210                 215                 220

Arg Leu Leu Phe Ser Ala Val Glu Trp Ala Arg Asn Ile Pro Phe Phe
225                 230                 235                 240

Pro Asp Leu Gln Ile Thr Asp Gln Val Ser Leu Leu Arg Leu Thr Trp
                245                 250                 255

Ser Glu Leu Phe Val Leu Asn Ala Ala Gln Cys Ser Met Pro Leu His
            260                 265                 270

Val Ala Pro Leu Leu Ala Ala Ala Gly Leu His Ala Ser Pro Met Ser
        275                 280                 285

Ala Asp Arg Val Val Ala Phe Met Asp His Ile Arg Ile Phe Gln Glu
    290                 295                 300

Gln Val Glu Lys Leu Lys Ala Leu His Val Asp Ser Ala Glu Tyr Ser
305                 310                 315                 320

Cys Leu Lys Ala Ile Val Leu Phe Thr Ser Asp Ala Cys Gly Leu Ser
                325                 330                 335

Asp Ala Ala His Ile Glu Ser Leu Gln Glu Lys Ser Gln Cys Ala Leu
            340                 345                 350

Glu Glu Tyr Val Arg Ser Gln Tyr Pro Asn Gln Pro Ser Arg Phe Gly
        355                 360                 365

Lys Leu Leu Leu Arg Leu Pro Ser Leu Arg Thr Val Ser Ser Ser Val
    370                 375                 380

Ile Glu Gln Leu Phe Phe Val Arg Leu Val Gly Lys Thr Pro Ile Glu
385                 390                 395                 400

Thr Leu Ile Arg Asp Met Leu Leu Ser Gly Ser Ser Phe Asn Trp Pro
                405                 410                 415

Tyr Met Ser Ile Gln Cys Ser
            420
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<210> 87

<211> 534
<212> PRT
<213> Homo sapiens

<400> 87

Met Ile Trp Tyr Ile Leu Ile Ile Gly Ile Leu Leu Pro Gln Ser Leu
1 5 10 15

Ala His Pro Gly Phe Phe Thr Ser Ile Gly Gln Met Thr Asp Leu Ile
20 25 30

His Thr Glu Lys Asp Leu Val Thr Ser Leu Lys Asp Tyr Ile Lys Ala
35 40 45

Glu Glu Asp Lys Leu Glu Gln Ile Lys Lys Trp Ala Glu Lys Leu Asp
50 55 60

Arg Leu Thr Ser Thr Ala Thr Lys Asp Pro Glu Gly Phe Val Gly His
65 70 75 80

Pro Val Asn Ala Phe Lys Leu Met Lys Arg Leu Asn Thr Glu Trp Ser
85 90 95

Glu Leu Glu Asn Leu Val Leu Lys Asp Met Ser Asp Gly Phe Ile Ser
100 105 110

Asn Leu Thr Ile Gln Arg Pro Val Leu Ser Asn Asp Glu Asp Gln Val
115 120 125

Gly Ala Ala Lys Ala Leu Leu Arg Leu Gln Asp Thr Tyr Asn Leu Asp
130 135 140

Thr Asp Thr Ile Ser Lys Gly Asn Leu Pro Gly Val Lys His Lys Ser
145 150 155 160

Phe Leu Thr Ala Glu Asp Cys Phe Glu Leu Gly Lys Val Ala Tyr Thr
165 170 175

Glu Ala Asp Tyr Tyr His Thr Glu Leu Trp Met Glu Gln Ala Leu Arg
180 185 190

Gln Leu Asp Glu Gly Glu Ile Ser Thr Ile Asp Lys Val Ser Val Leu
195 200 205

Asp Tyr Leu Ser Tyr Ala Val Tyr Gln Gln Gly Asp Leu Asp Lys Ala
210 215 220

Leu Leu Leu Thr Lys Lys Leu Leu Glu Leu Asp Pro Glu His Gln Arg
225 230 235 240

Ala Asn Gly Asn Leu Lys Tyr Phe Glu Tyr Ile Met Ala Lys Glu Lys
245 250 255

Asp Val Asn Lys Ser Ala Ser Asp Asp Gln Ser Asp Gln Lys Thr Thr
260 265 270

Pro Lys Lys Lys Gly Val Ala Val Asp Tyr Leu Pro Glu Arg Gln Lys
275 280 285

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Tyr Glu Met Leu Cys Arg Gly Glu Gly Ile Lys Met Thr Pro Arg Arg
    290                 295                 300

Gln Lys Lys Leu Phe Cys Arg Tyr His Asp Gly Asn Arg Asn Pro Lys
305                 310                 315                 320

Phe Ile Leu Ala Pro Ala Lys Gln Glu Asp Glu Trp Asp Lys Pro Arg
                325                 330                 335

Ile Ile Arg Phe His Asp Ile Ile Ser Asp Ala Glu Ile Glu Ile Val
            340                 345                 350

Lys Asp Leu Ala Lys Pro Arg Leu Ser Arg Ala Thr Val His Asp Pro
        355                 360                 365

Glu Thr Gly Lys Leu Thr Thr Ala Gln Tyr Arg Val Ser Lys Ser Ala
    370                 375                 380

Trp Leu Ser Gly Tyr Glu Asn Pro Val Val Ser Arg Ile Asn Met Arg
385                 390                 395                 400

Ile Gln Asp Leu Thr Gly Leu Asp Val Ser Thr Ala Glu Glu Leu Gln
                405                 410                 415

Val Ala Asn Tyr Gly Val Gly Gly Gln Tyr Glu Pro His Phe Asp Phe
            420                 425                 430

Ala Arg Lys Asp Glu Pro Asp Ala Phe Lys Glu Leu Gly Thr Gly Asn
        435                 440                 445

Arg Ile Ala Thr Trp Leu Phe Tyr Met Ser Asp Val Ser Ala Gly Gly
    450                 455                 460

Ala Thr Val Phe Pro Glu Val Gly Ala Ser Val Trp Pro Lys Lys Gly
465                 470                 475                 480

Thr Ala Val Phe Trp Tyr Asn Leu Phe Ala Ser Gly Glu Gly Asp Tyr
                485                 490                 495

Ser Thr Arg His Ala Ala Cys Pro Val Leu Val Gly Asn Lys Trp Val
            500                 505                 510

Ser Asn Lys Trp Leu His Glu Arg Gly Gln Glu Phe Arg Arg Pro Cys
        515                 520                 525

Thr Leu Ser Glu Leu Glu
    530

<210>  88
<211>  162
<212>  PRT
<213>  Homo sapiens

<400>  88

Met Asp Ile Pro Gln Thr Lys Gln Asp Leu Glu Leu Pro Lys Leu Ala
1               5                   10                  15

Gly Thr Trp His Ser Met Ala Met Ala Thr Asn Asn Ile Ser Leu Met
            20                  25                  30
```

Ala Thr Leu Lys Ala Pro Leu Arg Val His Ile Thr Ser Leu Leu Pro
35 40 45

Thr Pro Glu Asp Asn Leu Glu Ile Val Leu His Arg Trp Glu Asn Asn
50 55 60

Ser Cys Val Glu Lys Lys Val Leu Gly Glu Lys Thr Gly Asn Pro Lys
65 70 75 80

Lys Phe Lys Ile Asn Tyr Thr Val Ala Asn Glu Ala Thr Leu Leu Asp
85 90 95

Thr Asp Tyr Asp Asn Phe Leu Phe Leu Cys Leu Gln Asp Thr Thr Thr
100 105 110

Pro Ile Gln Ser Met Met Cys Gln Tyr Leu Ala Arg Val Leu Val Glu
115 120 125

Asp Asp Glu Ile Met Gln Gly Phe Ile Arg Ala Phe Arg Pro Leu Pro
130 135 140

Arg His Leu Trp Tyr Leu Leu Asp Leu Lys Gln Met Glu Glu Pro Cys
145 150 155 160

Arg Phe

<210> 89
<211> 449
<212> PRT
<213> Homo sapiens

<400> 89

Met Leu Pro Ala Ala Thr Ala Ser Leu Leu Gly Pro Leu Leu Thr Ala
1 5 10 15

Cys Ala Leu Leu Pro Phe Ala Gln Gly Gln Thr Pro Asn Tyr Thr Arg
20 25 30

Pro Val Phe Leu Cys Gly Gly Asp Val Lys Gly Glu Ser Gly Tyr Val
35 40 45

Ala Ser Glu Gly Phe Pro Asn Ser Tyr Pro Pro Asn Lys Glu Cys Ile
50 55 60

Trp Thr Ile Thr Val Pro Glu Gly Gln Thr Val Ser Leu Ser Phe Arg
65 70 75 80

Val Phe Asp Leu Glu Leu His Pro Ala Cys Arg Tyr Asp Ala Leu Glu
85 90 95

Val Phe Ala Gly Ser Gly Thr Ser Gly Gln Arg Leu Gly Arg Phe Cys
100 105 110

Gly Thr Phe Arg Pro Ala Pro Leu Val Ala Pro Gly Asn Gln Val Thr
115 120 125

Leu Arg Met Thr Thr Asp Glu Gly Thr Gly Gly Arg Gly Phe Leu Leu

130 135 140

Trp Tyr Ser Gly Arg Ala Thr Ser Gly Ser Glu His Gln Phe Cys Gly
145 150 155 160

Gly Arg Leu Glu Lys Ala Gln Gly Thr Leu Thr Thr Pro Asn Trp Pro
165 170 175

Glu Ser Asp Tyr Pro Pro Gly Ile Ser Cys Ser Trp His Ile Ile Ala
180 185 190

Pro Pro Asp Gln Val Ile Ala Leu Thr Phe Glu Lys Phe Asp Leu Glu
195 200 205

Pro Asp Thr Tyr Cys Arg Tyr Asp Ser Val Ser Val Phe Asn Gly Ala
210 215 220

Val Ser Asp Asp Ser Arg Arg Leu Gly Lys Phe Cys Gly Asp Ala Val
225 230 235 240

Pro Gly Ser Ile Ser Ser Glu Gly Asn Glu Leu Leu Val Gln Phe Val
245 250 255

Ser Asp Leu Ser Val Thr Ala Asp Gly Phe Ser Ala Ser Tyr Lys Thr
260 265 270

Leu Pro Arg Gly Thr Ala Lys Glu Gly Gln Gly Pro Gly Pro Lys Arg
275 280 285

Gly Thr Glu Pro Lys Val Lys Leu Pro Pro Lys Ser Gln Pro Pro Glu
290 295 300

Lys Thr Glu Glu Ser Pro Ser Ala Pro Asp Ala Pro Thr Cys Pro Lys
305 310 315 320

Gln Cys Arg Arg Thr Gly Thr Leu Gln Ser Asn Phe Cys Ala Ser Ser
325 330 335

Leu Val Val Thr Ala Thr Val Lys Ser Met Val Arg Glu Pro Gly Glu
340 345 350

Gly Leu Ala Val Thr Val Ser Leu Ile Gly Ala Tyr Lys Thr Gly Gly
355 360 365

Leu Asp Leu Pro Thr Pro Pro Thr Gly Ala Ser Leu Lys Phe Tyr Val
370 375 380

Pro Cys Lys Gln Cys Pro Pro Met Lys Lys Gly Val Ser Tyr Leu Leu
385 390 395 400

Met Gly Gln Val Glu Glu Asn Arg Gly Pro Val Leu Pro Pro Glu Ser
405 410 415

Phe Val Val Leu His Arg Pro Asn Gln Asp Gln Ile Leu Thr Asn Leu
420 425 430

Ser Lys Arg Lys Cys Pro Ser Gln Pro Val Arg Ala Ala Ala Ser Gln
435 440 445

Asp

<210> 90
<211> 1089
<212> PRT
<213> Homo sapiens

<400> 90

Met Gly Thr Ser His Pro Ala Phe Leu Val Leu Gly Cys Leu Leu Thr
1 5 10 15

Gly Leu Ser Leu Ile Leu Cys Gln Leu Ser Leu Pro Ser Ile Leu Pro
20 25 30

Asn Glu Asn Glu Lys Val Val Gln Leu Asn Ser Ser Phe Ser Leu Arg
35 40 45

Cys Phe Gly Glu Ser Glu Val Ser Trp Gln Tyr Pro Met Ser Glu Glu
50 55 60

Glu Ser Ser Asp Val Glu Ile Arg Asn Glu Glu Asn Asn Ser Gly Leu
65 70 75 80

Phe Val Thr Val Leu Glu Val Ser Ser Ala Ser Ala Ala His Thr Gly
85 90 95

Leu Tyr Thr Cys Tyr Tyr Asn His Thr Gln Thr Glu Glu Asn Glu Leu
100 105 110

Glu Gly Arg His Ile Tyr Ile Tyr Val Pro Asp Pro Asp Val Ala Phe
115 120 125

Val Pro Leu Gly Met Thr Asp Tyr Leu Val Ile Val Glu Asp Asp Asp
130 135 140

Ser Ala Ile Ile Pro Cys Arg Thr Thr Asp Pro Glu Thr Pro Val Thr
145 150 155 160

Leu His Asn Ser Glu Gly Val Val Pro Ala Ser Tyr Asp Ser Arg Gln
165 170 175

Gly Phe Asn Gly Thr Phe Thr Val Gly Pro Tyr Ile Cys Glu Ala Thr
180 185 190

Val Lys Gly Lys Lys Phe Gln Thr Ile Pro Phe Asn Val Tyr Ala Leu
195 200 205

Lys Ala Thr Ser Glu Leu Asp Leu Glu Met Glu Ala Leu Lys Thr Val
210 215 220

Tyr Lys Ser Gly Glu Thr Ile Val Val Thr Cys Ala Val Phe Asn Asn
225 230 235 240

Glu Val Val Asp Leu Gln Trp Thr Tyr Pro Gly Glu Val Lys Gly Lys
245 250 255

Gly Ile Thr Met Leu Glu Glu Ile Lys Val Pro Ser Ile Lys Leu Val
260 265 270

Tyr Thr Leu Thr Val Pro Glu Ala Thr Val Lys Asp Ser Gly Asp Tyr
275 280 285

Glu Cys Ala Ala Arg Gln Ala Thr Arg Glu Val Lys Glu Met Lys Lys
290 295 300

Val Thr Ile Ser Val His Glu Lys Gly Phe Ile Glu Ile Lys Pro Thr
305 310 315 320

Phe Ser Gln Leu Glu Ala Val Asn Leu His Glu Val Lys His Phe Val
325 330 335

Val Glu Val Arg Ala Tyr Pro Pro Pro Arg Ile Ser Trp Leu Lys Asn
340 345 350

Asn Leu Thr Leu Ile Glu Asn Leu Thr Glu Ile Thr Thr Asp Val Glu
355 360 365

Lys Ile Gln Glu Ile Arg Tyr Arg Ser Lys Leu Lys Leu Ile Arg Ala
370 375 380

Lys Glu Glu Asp Ser Gly His Tyr Thr Ile Val Ala Gln Asn Glu Asp
385 390 395 400

Ala Val Lys Ser Tyr Thr Phe Glu Leu Leu Thr Gln Val Pro Ser Ser
405 410 415

Ile Leu Asp Leu Val Asp Asp His His Gly Ser Thr Gly Gly Gln Thr
420 425 430

Val Arg Cys Thr Ala Glu Gly Thr Pro Leu Pro Asp Ile Glu Trp Met
435 440 445

Ile Cys Lys Asp Ile Lys Lys Cys Asn Asn Glu Thr Ser Trp Thr Ile
450 455 460

Leu Ala Asn Asn Val Ser Asn Ile Ile Thr Glu Ile His Ser Arg Asp
465 470 475 480

Arg Ser Thr Val Glu Gly Arg Val Thr Phe Ala Lys Val Glu Glu Thr
485 490 495

Ile Ala Val Arg Cys Leu Ala Lys Asn Leu Leu Gly Ala Glu Asn Arg
500 505 510

Glu Leu Lys Leu Val Ala Pro Thr Leu Arg Ser Glu Leu Thr Val Ala
515 520 525

Ala Ala Val Leu Val Leu Leu Val Ile Val Ile Ile Ser Leu Ile Val
530 535 540

Leu Val Val Ile Trp Lys Gln Lys Pro Arg Tyr Glu Ile Arg Trp Arg
545 550 555 560

Val Ile Glu Ser Ile Ser Pro Asp Gly His Glu Tyr Ile Tyr Val Asp
565 570 575

Pro Met Gln Leu Pro Tyr Asp Ser Arg Trp Glu Phe Pro Arg Asp Gly
580 585 590

Leu Val Leu Gly Arg Val Leu Gly Ser Gly Ala Phe Gly Lys Val Val
595 600 605

Glu Gly Thr Ala Tyr Gly Leu Ser Arg Ser Gln Pro Val Met Lys Val
610 615 620

Ala Val Lys Met Leu Lys Pro Thr Ala Arg Ser Ser Glu Lys Gln Ala
625 630 635 640

Leu Met Ser Glu Leu Lys Ile Met Thr His Leu Gly Pro His Leu Asn
645 650 655

Ile Val Asn Leu Leu Gly Ala Cys Thr Lys Ser Gly Pro Ile Tyr Ile
660 665 670

Ile Thr Glu Tyr Cys Phe Tyr Gly Asp Leu Val Asn Tyr Leu His Lys
675 680 685

Asn Arg Asp Ser Phe Leu Ser His His Pro Glu Lys Pro Lys Lys Glu
690 695 700

Leu Asp Ile Phe Gly Leu Asn Pro Ala Asp Glu Ser Thr Arg Ser Tyr
705 710 715 720

Val Ile Leu Ser Phe Glu Asn Asn Gly Asp Tyr Met Asp Met Lys Gln
725 730 735

Ala Asp Thr Thr Gln Tyr Val Pro Met Leu Glu Arg Lys Glu Val Ser
740 745 750

Lys Tyr Ser Asp Ile Gln Arg Ser Leu Tyr Asp Arg Pro Ala Ser Tyr
755 760 765

Lys Lys Lys Ser Met Leu Asp Ser Glu Val Lys Asn Leu Leu Ser Asp
770 775 780

Asp Asn Ser Glu Gly Leu Thr Leu Leu Asp Leu Leu Ser Phe Thr Tyr
785 790 795 800

Gln Val Ala Arg Gly Met Glu Phe Leu Ala Ser Lys Asn Cys Val His
805 810 815

Arg Asp Leu Ala Ala Arg Asn Val Leu Leu Ala Gln Gly Lys Ile Val
820 825 830

Lys Ile Cys Asp Phe Gly Leu Ala Arg Asp Ile Met His Asp Ser Asn
835 840 845

Tyr Val Ser Lys Gly Ser Thr Phe Leu Pro Val Lys Trp Met Ala Pro
850 855 860

Glu Ser Ile Phe Asp Asn Leu Tyr Thr Thr Leu Ser Asp Val Trp Ser
865 870 875 880

Tyr Gly Ile Leu Leu Trp Glu Ile Phe Ser Leu Gly Gly Thr Pro Tyr
885 890 895

Pro Gly Met Met Val Asp Ser Thr Phe Tyr Asn Lys Ile Lys Ser Gly
900 905 910

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Tyr Arg Met Ala Lys Pro Asp His Ala Thr Ser Glu Val Tyr Glu Ile
        915                 920                 925

Met Val Lys Cys Trp Asn Ser Glu Pro Glu Lys Arg Pro Ser Phe Tyr
    930                 935                 940

His Leu Ser Glu Ile Val Glu Asn Leu Leu Pro Gly Gln Tyr Lys Lys
945                 950                 955                 960

Ser Tyr Glu Lys Ile His Leu Asp Phe Leu Lys Ser Asp His Pro Ala
                965                 970                 975

Val Ala Arg Met Arg Val Asp Ser Asp Asn Ala Tyr Ile Gly Val Thr
            980                 985                 990

Tyr Lys Asn Glu Glu Asp Lys Leu Lys Asp Trp Glu Gly Gly Leu Asp
        995                1000                1005

Glu Gln Arg Leu Ser Ala Asp Ser Gly Tyr Ile Ile Pro Leu Pro
    1010                1015                1020

Asp Ile Asp Pro Val Pro Glu Glu Glu Asp Leu Gly Lys Arg Asn
    1025                1030                1035

Arg His Ser Ser Gln Thr Ser Glu Glu Ser Ala Ile Glu Thr Gly
    1040                1045                1050

Ser Ser Ser Ser Thr Phe Ile Lys Arg Glu Asp Glu Thr Ile Glu
    1055                1060                1065

Asp Ile Asp Met Met Asp Asp Ile Gly Ile Asp Ser Ser Asp Leu
    1070                1075                1080

Val Glu Asp Ser Phe Leu
    1085
```

<210> 91
<211> 318
<212> PRT
<213> Homo sapiens

<400> 91

```
Met Pro Asn Ile Lys Ile Phe Ser Gly Ser Ser His Gln Asp Leu Ser
1               5                  10                  15

Gln Lys Ile Ala Asp Arg Leu Gly Leu Glu Leu Gly Lys Val Val Thr
            20                  25                  30

Lys Lys Phe Ser Asn Gln Glu Thr Cys Val Glu Ile Gly Glu Ser Val
        35                  40                  45

Arg Gly Glu Asp Val Tyr Ile Val Gln Ser Gly Cys Gly Glu Ile Asn
    50                  55                  60

Asp Asn Leu Met Glu Leu Leu Ile Met Ile Asn Ala Cys Lys Ile Ala
65                  70                  75                  80

Ser Ala Ser Arg Val Thr Ala Val Ile Pro Cys Phe Pro Tyr Ala Arg
                85                  90                  95
```

Gln Asp Lys Lys Asp Lys Ser Arg Ala Pro Ile Ser Ala Lys Leu Val
100 105 110

Ala Asn Met Leu Ser Val Ala Gly Ala Asp His Ile Ile Thr Met Asp
115 120 125

Leu His Ala Ser Gln Ile Gln Gly Phe Phe Asp Ile Pro Val Asp Asn
130 135 140

Leu Tyr Ala Glu Pro Ala Val Leu Lys Trp Ile Arg Glu Asn Ile Ser
145 150 155 160

Glu Trp Arg Asn Cys Thr Ile Val Ser Pro Asp Ala Gly Gly Ala Lys
165 170 175

Arg Val Thr Ser Ile Ala Asp Arg Leu Asn Val Asp Phe Ala Leu Ile
180 185 190

His Lys Glu Arg Lys Lys Ala Asn Glu Val Asp Arg Met Val Leu Val
195 200 205

Gly Asp Val Lys Asp Arg Val Ala Ile Leu Val Asp Asp Met Ala Asp
210 215 220

Thr Cys Gly Thr Ile Cys His Ala Ala Asp Lys Leu Leu Ser Ala Gly
225 230 235 240

Ala Thr Arg Val Tyr Ala Ile Leu Thr His Gly Ile Phe Ser Gly Pro
245 250 255

Ala Ile Ser Arg Ile Asn Asn Ala Cys Phe Glu Ala Val Val Val Thr
260 265 270

Asn Thr Ile Pro Gln Glu Asp Lys Met Lys His Cys Ser Lys Ile Gln
275 280 285

Val Ile Asp Ile Ser Met Ile Leu Ala Glu Ala Ile Arg Arg Thr His
290 295 300

Asn Gly Glu Ser Val Ser Tyr Leu Phe Ser His Val Pro Leu
305 310 315

<210> 92
<211> 318
<212> PRT
<213> Homo sapiens

<400> 92

Met Pro Asn Ile Val Leu Phe Ser Gly Ser Ser His Gln Asp Leu Ser
1 5 10 15

Gln Arg Val Ala Asp Arg Leu Gly Leu Glu Leu Gly Lys Val Val Thr
20 25 30

Lys Lys Phe Ser Asn Gln Glu Thr Ser Val Glu Ile Gly Glu Ser Val
35 40 45

Arg Gly Glu Asp Val Tyr Ile Ile Gln Ser Gly Cys Gly Glu Ile Asn

50 55 60

Asp Asn Leu Met Glu Leu Leu Ile Met Ile Asn Ala Cys Lys Ile Ala
65 70 75 80

Ser Ser Ser Arg Val Thr Ala Val Ile Pro Cys Phe Pro Tyr Ala Arg
85 90 95

Gln Asp Lys Lys Asp Lys Ser Arg Ala Pro Ile Ser Ala Lys Leu Val
100 105 110

Ala Asn Met Leu Ser Val Ala Gly Ala Asp His Ile Ile Thr Met Asp
115 120 125

Leu His Ala Ser Gln Ile Gln Gly Phe Phe Asp Ile Pro Val Asp Asn
130 135 140

Leu Tyr Ala Glu Pro Ala Val Leu Gln Trp Ile Arg Glu Asn Ile Ala
145 150 155 160

Glu Trp Lys Asn Cys Ile Ile Val Ser Pro Asp Ala Gly Gly Ala Lys
165 170 175

Arg Val Thr Ser Ile Ala Asp Arg Leu Asn Val Glu Phe Ala Leu Ile
180 185 190

His Lys Glu Arg Lys Lys Ala Asn Glu Val Asp Arg Met Val Leu Val
195 200 205

Gly Asp Val Lys Asp Arg Val Ala Ile Leu Val Asp Asp Met Ala Asp
210 215 220

Thr Cys Gly Thr Ile Cys His Ala Ala Asp Lys Leu Leu Ser Ala Gly
225 230 235 240

Ala Thr Lys Val Tyr Ala Ile Leu Thr His Gly Ile Phe Ser Gly Pro
245 250 255

Ala Ile Ser Arg Ile Asn Asn Ala Ala Phe Glu Ala Val Val Val Thr
260 265 270

Asn Thr Ile Pro Gln Glu Asp Lys Met Lys His Cys Thr Lys Ile Gln
275 280 285

Val Ile Asp Ile Ser Met Ile Leu Ala Glu Ala Ile Arg Arg Thr His
290 295 300

Asn Gly Glu Ser Val Ser Tyr Leu Phe Ser His Val Pro Leu
305 310 315

<210> 93
<211> 244
<212> PRT
<213> Homo sapiens

<400> 93

Met Ala Ala Ala Ala Ala Ala Gly Glu Ala Arg Arg Val Leu Val Tyr
1 5 10 15

Gly Gly Arg Gly Ala Leu Gly Ser Arg Cys Val Gln Ala Phe Arg Ala
20 25 30

Arg Asn Trp Trp Val Ala Ser Val Asp Val Val Glu Asn Glu Glu Ala
35 40 45

Ser Ala Thr Ile Ile Val Lys Met Thr Asp Ser Phe Thr Glu Gln Ala
50 55 60

Asp Gln Val Thr Ala Glu Val Gly Lys Leu Leu Gly Glu Glu Lys Val
65 70 75 80

Asp Ala Ile Leu Cys Val Ala Gly Gly Trp Ala Gly Gly Asn Ala Lys
85 90 95

Ser Lys Ser Leu Phe Lys Asn Cys Asp Leu Met Trp Lys Gln Ser Ile
100 105 110

Trp Thr Ser Thr Ile Ser Ser His Leu Ala Thr Lys His Leu Lys Glu
115 120 125

Gly Gly Leu Leu Thr Leu Ala Gly Ala Lys Ala Ala Leu Asp Gly Thr
130 135 140

Pro Gly Met Ile Gly Tyr Gly Met Ala Lys Gly Ala Val His Gln Leu
145 150 155 160

Cys Gln Ser Leu Ala Gly Lys Asn Ser Gly Met Pro Pro Gly Ala Ala
165 170 175

Ala Ile Ala Val Leu Pro Val Thr Leu Asp Thr Pro Met Asn Arg Lys
180 185 190

Ser Met Pro Glu Ala Asp Phe Ser Ser Trp Thr Pro Leu Glu Phe Leu
195 200 205

Val Glu Thr Phe His Asp Trp Ile Thr Gly Lys Asn Arg Pro Ser Ser
210 215 220

Gly Ser Leu Ile Gln Val Val Thr Thr Glu Gly Arg Thr Glu Leu Thr
225 230 235 240

Pro Ala Tyr Phe

<210> 94
<211> 331
<212> PRT
<213> Homo sapiens

<400> 94

Met Gly Thr Pro Gln Lys Asp Val Ile Ile Lys Ser Asp Ala Pro Asp
1 5 10 15

Thr Leu Leu Leu Glu Lys His Ala Asp Tyr Ile Ala Ser Tyr Gly Ser
20 25 30

Lys Lys Asp Asp Tyr Glu Tyr Cys Met Ser Glu Tyr Leu Arg Met Ser
35 40 45

```
Gly Ile Tyr Trp Gly Leu Thr Val Met Asp Leu Met Gly Gln Leu His
    50                  55                  60

Arg Met Asn Arg Glu Glu Ile Leu Ala Phe Ile Lys Ser Cys Gln His
65                  70                  75                  80

Glu Cys Gly Gly Ile Ser Ala Ser Ile Gly His Asp Pro His Leu Leu
                85                  90                  95

Tyr Thr Leu Ser Ala Val Gln Ile Leu Thr Leu Tyr Asp Ser Ile Asn
            100                 105                 110

Val Ile Asp Val Asn Lys Val Val Glu Tyr Val Lys Gly Leu Gln Lys
        115                 120                 125

Glu Asp Gly Ser Phe Ala Gly Asp Ile Trp Gly Glu Ile Asp Thr Arg
    130                 135                 140

Phe Ser Phe Cys Ala Val Ala Thr Leu Ala Leu Leu Gly Lys Leu Asp
145                 150                 155                 160

Ala Ile Asn Val Glu Lys Ala Ile Glu Phe Val Leu Ser Cys Met Asn
                165                 170                 175

Phe Asp Gly Gly Phe Gly Cys Arg Pro Gly Ser Glu Ser His Ala Gly
            180                 185                 190

Gln Ile Tyr Cys Cys Thr Gly Phe Leu Ala Ile Thr Ser Gln Leu His
        195                 200                 205

Gln Val Asn Ser Asp Leu Leu Gly Trp Trp Leu Cys Glu Arg Gln Leu
    210                 215                 220

Pro Ser Gly Gly Leu Asn Gly Arg Pro Glu Lys Leu Pro Asp Val Cys
225                 230                 235                 240

Tyr Ser Trp Trp Val Leu Ala Ser Leu Lys Ile Ile Gly Arg Leu His
                245                 250                 255

Trp Ile Asp Arg Glu Lys Leu Arg Asn Phe Ile Leu Ala Cys Gln Asp
            260                 265                 270

Glu Glu Thr Gly Gly Phe Ala Asp Arg Pro Gly Asp Met Val Asp Pro
        275                 280                 285

Phe His Thr Leu Phe Gly Ile Ala Gly Leu Ser Leu Leu Gly Glu Glu
    290                 295                 300

Gln Ile Lys Pro Val Asn Pro Val Phe Cys Met Pro Glu Glu Val Leu
305                 310                 315                 320

Gln Arg Val Asn Val Gln Pro Glu Leu Val Ser
                325                 330
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<210> 95
<211> 93
<212> PRT
<213> Homo sapiens

<400> 95

Met Asn Ala Lys Val Val Val Val Leu Val Leu Val Leu Thr Ala Leu
1 5 10 15

Cys Leu Ser Asp Gly Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys
20 25 30

Arg Phe Phe Glu Ser His Val Ala Arg Ala Asn Val Lys His Leu Lys
35 40 45

Ile Leu Asn Thr Pro Asn Cys Ala Leu Gln Ile Val Ala Arg Leu Lys
50 55 60

Asn Asn Asn Arg Gln Val Cys Ile Asp Pro Lys Leu Lys Trp Ile Gln
65 70 75 80

Glu Tyr Leu Glu Lys Ala Leu Asn Lys Arg Phe Lys Met
85 90

<210> 96
<211> 381
<212> PRT
<213> Homo sapiens

<220>
<221> UNSURE
<222> (59)..(59)
<223> Xaa = any amino acid

<220>
<221> UNSURE
<222> (300)..(300)
<223> Xaa = any amino acid

<220>
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<222> (318)..(318)
<223> Xaa = any amino acid

<220>
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<222> (330)..(330)
<223> Xaa = any amino acid

<220>
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<222> (345)..(345)
<223> Xaa = any amino acid

<220>
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<223> Xaa = any amino acid

<220>
<221> UNSURE
<222> (367)..(367)
<223> Xaa = any amino acid

<220>
<221> UNSURE
<222> (369)..(369)
<223> Xaa = any amino acid

<220>
<221> UNSURE
<222> (376)..(376)
<223> Xaa = any amino acid

<220>
<221> UNSURE
<222> (378)..(378)
<223> Xaa = any amino acid

<400> 96

Met Trp Arg Ser Leu Gly Leu Ala Leu Ala Leu Cys Leu Leu Pro Ser
1 5 10 15

Gly Gly Thr Glu Ser Gln Asp Gln Ser Ser Leu Cys Lys Gln Pro Pro
20 25 30

Ala Trp Ser Ile Arg Asp Gln Asp Pro Met Leu Asn Ser Asn Gly Ser
35 40 45

Val Thr Val Val Ala Leu Leu Gln Ala Ser Xaa Tyr Leu Cys Ile Ile
50 55 60

Glu Ala Ser Lys Leu Glu Asp Leu Arg Val Lys Leu Lys Lys Glu Gly
65 70 75 80

Tyr Ser Asn Ile Ser Tyr Ile Val Val Asn His Gln Gly Ile Ser Ser
85 90 95

Arg Leu Lys Tyr Thr His Leu Lys Asn Lys Val Ser Glu His Ile Pro
100 105 110

Val Tyr Gln Gln Glu Glu Asn Gln Thr Asp Val Trp Thr Leu Leu Asn
115 120 125

Gly Ser Lys Asp Asp Phe Leu Ile Tyr Asp Arg Cys Gly Arg Leu Val
130 135 140

Tyr His Leu Gly Leu Pro Phe Ser Phe Leu Thr Phe Pro Tyr Val Glu
145 150 155 160

Glu Ala Ile Lys Ile Ala Tyr Cys Glu Lys Lys Cys Gly Asn Cys Ser
165 170 175

Leu Thr Thr Leu Lys Asp Glu Asp Phe Cys Lys Arg Val Ser Leu Ala
180 185 190

Thr Val Asp Lys Thr Val Glu Thr Pro Ser Pro His Tyr His His Glu
195 200 205

His His His Asn His Gly His Gln His Leu Gly Ser Ser Glu Leu Ser
210 215 220

Glu Asn Gln Gln Pro Gly Ala Pro Asn Ala Pro Thr His Pro Ala Pro
225 230 235 240

Pro Gly Leu His His His His Lys His Lys Gly Gln His Arg Gln Gly
245 250 255

His Pro Glu Asn Arg Asp Met Pro Ala Ser Glu Asp Leu Gln Asp Leu
260 265 270

Gln Lys Lys Leu Cys Arg Lys Arg Cys Ile Asn Gln Leu Leu Cys Lys
275 280 285

Leu Pro Thr Asp Ser Glu Leu Ala Pro Arg Ser Xaa Cys Cys His Cys
290 295 300

Arg His Leu Ile Phe Glu Lys Thr Gly Ser Ala Ile Thr Xaa Gln Cys
305 310 315 320

Lys Glu Asn Leu Pro Ser Leu Cys Ser Xaa Gln Gly Leu Arg Ala Glu
325 330 335

Glu Asn Ile Thr Glu Ser Cys Gln Xaa Arg Leu Pro Pro Ala Ala Xaa
340 345 350

Gln Ile Ser Gln Gln Leu Ile Pro Thr Glu Ala Ser Ala Ser Xaa Arg
355 360 365

Xaa Lys Asn Gln Ala Lys Lys Xaa Glu Xaa Pro Ser Asn
370 375 380

<210> 97
<211> 220
<212> PRT
<213> Homo sapiens

<400> 97

Met Ala Ile Leu Phe Ala Val Val Ala Arg Gly Thr Thr Ile Leu Ala
1 5 10 15

Lys His Ala Trp Cys Gly Gly Asn Phe Leu Glu Val Thr Glu Gln Ile
20 25 30

Leu Ala Lys Ile Pro Ser Glu Asn Asn Lys Leu Thr Tyr Ser His Gly
35 40 45

Asn Tyr Leu Phe His Tyr Ile Cys Gln Asp Arg Ile Val Tyr Leu Cys
50 55 60

Ile Thr Asp Asp Asp Phe Glu Arg Ser Arg Ala Phe Asn Phe Leu Asn
65 70 75 80

Glu Ile Lys Lys Arg Phe Gln Thr Thr Tyr Gly Ser Arg Ala Gln Thr
85 90 95

Ala Leu Pro Tyr Ala Met Asn Ser Glu Phe Ser Ser Val Leu Ala Ala
100 105 110

Gln Leu Lys His His Ser Glu Asn Lys Gly Leu Asp Lys Val Met Glu
115 120 125

Thr Gln Ala Gln Val Asp Glu Leu Lys Gly Ile Met Val Arg Asn Ile
130 135 140

Asp Leu Val Ala Gln Arg Gly Glu Arg Leu Glu Leu Leu Ile Asp Lys
145 150 155 160

Thr Glu Asn Leu Val Asp Ser Ser Val Thr Phe Lys Thr Thr Ser Arg
165 170 175

Asn Leu Ala Arg Ala Met Cys Met Lys Asn Leu Lys Leu Thr Ile Ile
180 185 190

Ile Ile Ile Val Ser Ile Val Phe Ile Tyr Ile Ile Val Ser Pro Leu
195 200 205

Cys Gly Gly Phe Thr Trp Pro Ser Cys Val Lys Lys
210 215 220

<210> 98
<211> 1736
<212> PRT
<213> Homo sapiens

<400> 98

Met Glu Glu Thr Ala Ile Trp Glu Gln His Thr Val Thr Leu His Arg
1 5 10 15

Ala Pro Gly Phe Gly Phe Gly Ile Ala Ile Ser Gly Gly Arg Asp Asn
20 25 30

Pro His Phe Gln Ser Gly Glu Thr Ser Ile Val Ile Ser Asp Val Leu
35 40 45

Lys Gly Gly Pro Ala Glu Gly Gln Leu Gln Glu Asn Asp Arg Val Ala
50 55 60

Met Val Asn Gly Val Ser Met Asp Asn Val Glu His Ala Phe Ala Val
65 70 75 80

Gln Gln Leu Arg Lys Ser Gly Lys Asn Ala Lys Ile Thr Ile Arg Arg
85 90 95

Lys Lys Lys Val Gln Ile Pro Val Ser Arg Pro Asp Pro Glu Pro Val
100 105 110

Ser Asp Asn Glu Glu Asp Ser Tyr Asp Glu Glu Ile His Asp Pro Arg
115 120 125

Ser Gly Arg Ser Gly Val Val Asn Arg Arg Ser Glu Lys Ile Trp Pro

130 135 140

Arg Asp Arg Ser Ala Ser Arg Glu Arg Ser Leu Ser Pro Arg Ser Asp
145 150 155 160

Arg Arg Ser Val Ala Ser Ser Gln Pro Ala Lys Pro Thr Lys Val Thr
165 170 175

Leu Val Lys Ser Arg Lys Asn Glu Glu Tyr Gly Leu Arg Leu Ala Ser
180 185 190

His Ile Phe Val Lys Glu Ile Ser Gln Asp Ser Leu Ala Ala Arg Asp
195 200 205

Gly Asn Ile Gln Glu Gly Asp Val Val Leu Lys Ile Asn Gly Thr Val
210 215 220

Thr Glu Asn Met Ser Leu Thr Asp Ala Lys Thr Leu Ile Glu Arg Ser
225 230 235 240

Lys Gly Lys Leu Lys Met Val Val Gln Arg Asp Glu Arg Ala Thr Leu
245 250 255

Leu Asn Val Pro Asp Leu Ser Asp Ser Ile His Ser Ala Asn Ala Ser
260 265 270

Glu Arg Asp Asp Ile Ser Glu Ile Gln Ser Leu Ala Ser Asp His Ser
275 280 285

Gly Arg Ser His Asp Arg Pro Pro Arg Arg Ser Arg Ser Arg Ser Pro
290 295 300

Asp Gln Arg Ser Glu Pro Ser Asp His Ser Arg His Ser Pro Gln Gln
305 310 315 320

Pro Ser Asn Gly Ser Leu Arg Ser Arg Asp Glu Glu Arg Ile Ser Lys
325 330 335

Pro Gly Ala Val Ser Thr Pro Val Lys His Ala Asp Asp His Thr Pro
340 345 350

Lys Thr Val Glu Glu Val Thr Val Glu Arg Asn Glu Lys Gln Thr Pro
355 360 365

Ser Leu Pro Glu Pro Lys Pro Val Tyr Ala Gln Val Gly Asn Gln Met
370 375 380

Trp Ile Tyr Leu Ser Val His Leu Met Val Ser Tyr Leu Ile Gln Leu
385 390 395 400

Met Lys Met Gly Phe Leu Arg Pro Ser Met Lys Leu Val Lys Phe Arg
405 410 415

Lys Gly Asp Ser Val Gly Leu Arg Leu Ala Gly Gly Asn Asp Val Gly
420 425 430

Ile Phe Val Ala Gly Val Leu Glu Asp Ser Pro Ala Ala Lys Glu Gly
435 440 445

Leu Glu Glu Gly Asp Gln Ile Leu Arg Val Asn Asn Val Asp Phe Thr

450 455 460

Asn Ile Ile Arg Glu Glu Ala Val Leu Phe Leu Leu Asp Leu Pro Lys
465 470 475 480

Gly Glu Glu Val Thr Ile Leu Ala Gln Lys Lys Lys Asp Val Tyr Arg
485 490 495

Arg Ile Val Glu Ser Asp Val Gly Asp Ser Phe Tyr Ile Arg Thr His
500 505 510

Phe Glu Tyr Glu Lys Glu Ser Pro Tyr Gly Leu Ser Phe Asn Lys Gly
515 520 525

Glu Val Phe Arg Ala Val Asp Thr Leu Tyr Asn Gly Lys Leu Gly Ser
530 535 540

Trp Leu Ala Ile Arg Ile Gly Lys Asn His Lys Glu Val Glu Arg Gly
545 550 555 560

Ile Ile Pro Asn Lys Asn Arg Ala Glu Gln Leu Ala Ser Val Gln Tyr
565 570 575

Thr Leu Pro Lys Thr Ala Gly Gly Asp Arg Ala Asp Phe Trp Arg Phe
580 585 590

Arg Gly Leu Arg Ser Ser Lys Arg Asn Leu Arg Lys Ser Arg Glu Asp
595 600 605

Leu Ser Ala Gln Pro Val Gln Thr Lys Phe Pro Ala Tyr Glu Arg Val
610 615 620

Val Leu Arg Glu Ala Gly Phe Leu Arg Pro Val Thr Ile Phe Gly Pro
625 630 635 640

Ile Ala Asp Val Ala Arg Glu Lys Leu Ala Arg Glu Glu Pro Asp Ile
645 650 655

Tyr Gln Ile Ala Lys Ser Glu Pro Arg Asp Ala Gly Thr Asp Gln Arg
660 665 670

Ser Ser Gly Tyr Ile Arg Leu His Thr Ile Lys Gln Ile Ile Asp Gln
675 680 685

Asp Lys His Ala Leu Leu Asp Val Thr Pro Asn Ala Val Asp Arg Leu
690 695 700

Asn Tyr Ala Gln Trp Tyr Pro Ile Val Val Phe Leu Asn Pro Asp Ser
705 710 715 720

Lys Gln Gly Val Lys Thr Met Arg Met Arg Leu Cys Pro Glu Ser Arg
725 730 735

Lys Ser Ala Arg Lys Leu Tyr Glu Arg Ser His Lys Leu Ala Lys Asn
740 745 750

Asn His His Leu Phe Thr Thr Thr Ile Asn Leu Asn Ser Met Asn Asp
755 760 765

Gly Trp Tyr Gly Ala Leu Lys Glu Ala Val Gln Gln Gln Gln Asn Gln

770 775 780

Leu Val Trp Val Ser Glu Gly Lys Ala Asp Gly Ala Thr Ser Asp Asp
785 790 795 800

Leu Asp Leu His Asp Asp Arg Leu Ser Tyr Leu Ser Ala Pro Gly Ser
805 810 815

Glu Tyr Ser Met Tyr Ser Thr Asp Ser Arg His Thr Ser Asp Tyr Glu
820 825 830

Asp Thr Asp Thr Glu Gly Gly Ala Tyr Thr Asp Gln Glu Leu Asp Glu
835 840 845

Thr Leu Asn Asp Glu Val Gly Thr Pro Pro Glu Ser Ala Ile Thr Arg
850 855 860

Ser Ser Glu Pro Val Arg Glu Asp Ser Ser Gly Met His His Glu Asn
865 870 875 880

Gln Thr Tyr Pro Pro Tyr Ser Pro Gln Ala Gln Pro Gln Pro Ile His
885 890 895

Arg Ile Asp Ser Pro Gly Phe Lys Pro Ala Ser Gln Gln Lys Ala Glu
900 905 910

Ala Ser Ser Pro Val Pro Tyr Leu Ser Pro Glu Thr Asn Pro Ala Ser
915 920 925

Ser Thr Ser Ala Val Asn His Asn Val Asn Leu Thr Asn Val Arg Leu
930 935 940

Glu Glu Pro Thr Pro Ala Pro Ser Thr Ser Tyr Ser Pro Gln Ala Asp
945 950 955 960

Ser Leu Arg Thr Pro Ser Thr Glu Ala Ala His Ile Met Leu Arg Asp
965 970 975

Gln Glu Pro Ser Leu Ser Ser His Val Asp Pro Thr Lys Val Tyr Arg
980 985 990

Lys Asp Pro Tyr Pro Glu Glu Met Met Arg Gln Asn His Val Leu Lys
995 1000 1005

Gln Pro Ala Val Ser His Pro Gly His Arg Pro Asp Lys Glu Pro
1010 1015 1020

Asn Leu Thr Tyr Glu Pro Gln Leu Pro Tyr Val Glu Lys Gln Ala
1025 1030 1035

Ser Arg Asp Leu Glu Gln Pro Thr Tyr Arg Tyr Glu Ser Ser Ser
1040 1045 1050

Tyr Thr Asp Gln Phe Ser Arg Asn Tyr Glu His Arg Leu Arg Tyr
1055 1060 1065

Glu Asp Arg Val Pro Met Tyr Glu Glu Gln Trp Ser Tyr Tyr Asp
1070 1075 1080

Asp Lys Gln Pro Tyr Pro Ser Arg Pro Pro Phe Asp Asn Gln His

1085 1090 1095

Ser Gln Asp Leu Asp Ser Arg Gln His Pro Glu Glu Ser Ser Glu
1100 1105 1110

Arg Gly Tyr Phe Pro Arg Phe Glu Glu Pro Ala Pro Leu Ser Tyr
1115 1120 1125

Asp Ser Arg Pro Arg Tyr Glu Gln Ala Pro Arg Ala Ser Ala Leu
1130 1135 1140

Arg His Glu Glu Gln Pro Ala Pro Gly Tyr Asp Thr His Gly Arg
1145 1150 1155

Leu Arg Pro Glu Ala Gln Pro His Pro Ser Ala Gly Pro Lys Pro
1160 1165 1170

Ala Glu Ser Lys Gln Tyr Phe Glu Gln Tyr Ser Arg Ser Tyr Glu
1175 1180 1185

Gln Val Pro Pro Gln Gly Phe Thr Ser Arg Ala Gly His Phe Glu
1190 1195 1200

Pro Leu His Gly Ala Ala Ala Val Pro Pro Leu Ile Pro Ser Ser
1205 1210 1215

Gln His Lys Pro Glu Ala Leu Pro Ser Asn Thr Lys Pro Leu Pro
1220 1225 1230

Pro Pro Pro Thr Gln Thr Glu Glu Glu Glu Asp Pro Ala Met Lys
1235 1240 1245

Pro Gln Ser Val Leu Thr Arg Val Lys Met Phe Glu Asn Lys Arg
1250 1255 1260

Ser Ala Ser Leu Glu Thr Lys Lys Asp Val Asn Asp Thr Gly Ser
1265 1270 1275

Phe Lys Pro Pro Glu Val Ala Ser Lys Pro Ser Gly Ala Pro Ile
1280 1285 1290

Ile Gly Pro Lys Pro Thr Ser Gln Asn Gln Phe Ser Glu His Asp
1295 1300 1305

Lys Thr Leu Tyr Arg Ile Pro Glu Pro Gln Lys Pro Gln Leu Lys
1310 1315 1320

Pro Pro Glu Asp Ile Val Arg Ser Asn His Tyr Asp Pro Glu Glu
1325 1330 1335

Asp Glu Glu Tyr Tyr Arg Lys Gln Leu Ser Tyr Phe Asp Arg Arg
1340 1345 1350

Ser Phe Glu Asn Lys Pro Pro Ala His Ile Ala Ala Ser His Leu
1355 1360 1365

Ser Glu Pro Ala Lys Pro Ala His Ser Gln Asn Gln Ser Asn Phe
1370 1375 1380

Ser Ser Tyr Ser Ser Lys Gly Lys Pro Pro Glu Ala Asp Gly Val

1385 1390 1395

Asp Arg Ser Phe Gly Glu Lys Arg Tyr Glu Pro Ile Gln Ala Thr
1400 1405 1410

Pro Pro Pro Pro Pro Leu Pro Ser Gln Tyr Ala Gln Pro Ser Gln
1415 1420 1425

Pro Val Thr Ser Ala Ser Leu His Ile His Ser Lys Gly Ala His
1430 1435 1440

Gly Glu Gly Asn Ser Val Ser Leu Asp Phe Gln Asn Ser Leu Val
1445 1450 1455

Ser Lys Pro Asp Pro Pro Pro Ser Gln Asn Lys Pro Ala Thr Phe
1460 1465 1470

Arg Pro Pro Asn Arg Glu Asp Thr Ala Gln Ala Ala Phe Tyr Pro
1475 1480 1485

Gln Lys Ser Phe Pro Asp Lys Ala Pro Val Asn Gly Thr Glu Gln
1490 1495 1500

Thr Gln Lys Thr Val Thr Pro Ala Tyr Asn Arg Phe Thr Pro Lys
1505 1510 1515

Pro Tyr Thr Ser Ser Ala Arg Pro Phe Glu Arg Lys Phe Glu Ser
1520 1525 1530

Pro Lys Phe Asn His Asn Leu Leu Pro Ser Glu Thr Ala His Lys
1535 1540 1545

Pro Asp Leu Ser Ser Lys Thr Pro Thr Ser Pro Lys Thr Leu Val
1550 1555 1560

Lys Ser His Ser Leu Ala Gln Pro Pro Glu Phe Asp Ser Gly Val
1565 1570 1575

Glu Thr Phe Ser Ile His Ala Glu Lys Pro Lys Tyr Gln Ile Asn
1580 1585 1590

Asn Ile Ser Thr Val Pro Lys Ala Ile Pro Val Ser Pro Ser Ala
1595 1600 1605

Val Glu Glu Asp Glu Asp Glu Asp Gly His Thr Val Val Ala Thr
1610 1615 1620

Ala Arg Gly Ile Phe Asn Ser Asn Gly Gly Val Leu Ser Ser Ile
1625 1630 1635

Glu Thr Gly Val Ser Ile Ile Ile Pro Gln Gly Ala Ile Pro Glu
1640 1645 1650

Gly Val Glu Gln Glu Ile Tyr Phe Lys Val Cys Arg Asp Asn Ser
1655 1660 1665

Ile Leu Pro Pro Leu Asp Lys Glu Lys Gly Glu Thr Leu Leu Ser
1670 1675 1680

Pro Leu Val Met Cys Gly Pro His Gly Leu Lys Phe Leu Lys Pro

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    1685                    1690                    1695

Val Glu  Leu Arg Leu Pro His  Cys Asp Pro Lys Thr  Trp Gln Asn
    1700                    1705                    1710

Lys Cys  Leu Pro Gly Asp Pro  Asn Tyr Leu Val Gly  Ala Asn Cys
    1715                    1720                    1725

Val Ser  Val Leu Ile Asp His  Phe
    1730                    1735

<210>  99
<211>  93
<212>  PRT
<213>  Homo sapiens

<400>  99

Met Gln Arg Arg Gly Gln Pro Leu Glu Asn His Val Ala Leu Ile His
1               5                   10                  15

Trp Gln Ser Ala Gly Ile Pro Ala Ser Lys Val His Asn Tyr Cys Asn
            20                  25                  30

Met Lys Lys Ser Arg Leu Gly Arg Ser Arg Ala Val Arg Ile Ser Gln
        35                  40                  45

Pro Leu Leu Ser Pro Arg Arg Cys Pro Leu His Leu Thr Glu Arg Gly
    50                  55                  60

Ala Gly Leu Leu Gln Pro Gln Pro Gln Gly Pro Val Arg Thr Pro Gly
65                  70                  75                  80

Pro Pro Pro Gly Val Thr Gln Arg Pro Arg Thr Thr Glu
                85                  90

<210>  100
<211>  582
<212>  PRT
<213>  Homo sapiens

<400>  100

Asp Val Ser Arg Cys Ala His Arg Ala Arg Pro Gly Ala Ile Met Leu
1               5                   10                  15

Leu Leu Pro Ser Ala Ala Asp Gly Arg Gly Thr Ala Ile Thr His Ala
            20                  25                  30

Leu Thr Ser Ala Ser Thr Leu Cys Gln Val Glu Pro Val Gly Arg Trp
        35                  40                  45

Phe Glu Ala Phe Val Lys Arg Arg Asn Arg Asn Ala Ser Ala Ser Phe
    50                  55                  60

Gln Glu Leu Glu Asp Lys Lys Glu Leu Ser Glu Glu Ser Glu Asp Glu
65                  70                  75                  80

Glu Leu Gln Leu Glu Glu Phe Pro Met Leu Lys Thr Leu Asp Pro Lys
                85                  90                  95
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Asp Trp Lys Asn Gln Asp His Tyr Ala Val Leu Gly Leu Gly His Val
100 105 110

Arg Tyr Lys Ala Thr Gln Arg Gln Ile Lys Ala Ala His Lys Ala Met
115 120 125

Val Leu Lys His His Pro Asp Lys Arg Lys Ala Ala Gly Glu Pro Ile
130 135 140

Lys Glu Gly Asp Asn Asp Tyr Phe Thr Cys Ile Thr Lys Ala Tyr Glu
145 150 155 160

Met Leu Ser Asp Pro Val Lys Arg Arg Ala Phe Asn Ser Val Asp Pro
165 170 175

Thr Phe Asp Asn Ser Val Pro Ser Lys Ser Glu Ala Lys Asp Asn Phe
180 185 190

Phe Glu Val Phe Thr Pro Val Phe Glu Arg Asn Ser Arg Trp Ser Asn
195 200 205

Lys Lys Asn Val Pro Lys Leu Gly Asp Met Asn Ser Ser Phe Glu Asp
210 215 220

Val Asp Ile Phe Tyr Ser Phe Trp Tyr Asn Phe Asp Ser Trp Arg Glu
225 230 235 240

Phe Ser Tyr Leu Asp Glu Glu Glu Lys Glu Lys Ala Glu Cys Arg Asp
245 250 255

Glu Arg Arg Trp Ile Glu Lys Gln Asn Gly Ala Thr Arg Ala Gln Arg
260 265 270

Lys Lys Glu Glu Met Asn Arg Ile Arg Thr Leu Val Asp Asn Ala Tyr
275 280 285

Ser Cys Asp Pro Arg Ile Lys Lys Phe Lys Glu Glu Glu Lys Ala Lys
290 295 300

Lys Glu Ala Glu Lys Lys Ala Lys Ala Glu Ala Lys Arg Lys Glu Gln
305 310 315 320

Glu Ala Lys Glu Lys Gln Arg Gln Ala Glu Leu Glu Ala Ala Arg Leu
325 330 335

Ala Lys Glu Lys Glu Glu Glu Glu Val Arg Gln Gln Ala Leu Leu Ala
340 345 350

Lys Lys Glu Lys Asp Ile Gln Lys Lys Ala Ile Lys Lys Glu Arg Gln
355 360 365

Lys Leu Arg Asn Ser Cys Lys Ile Glu Glu Ile Asn Glu Gln Ile Arg
370 375 380

Lys Glu Lys Glu Glu Ala Glu Ala Arg Met Arg Gln Ala Ser Lys Asn
385 390 395 400

Thr Glu Lys Ser Thr Gly Gly Gly Gly Asn Gly Ser Lys Asn Trp Ser
405 410 415

Glu Asp Asp Leu Gln Leu Leu Ile Lys Ala Val Asn Leu Phe Pro Ala
420 425 430

Arg Thr Asn Ser Arg Trp Glu Val Ile Ala Asn Tyr Met Asn Ile His
435 440 445

Ser Ser Ser Gly Val Lys Arg Thr Ala Lys Asp Val Ile Gly Lys Ala
450 455 460

Lys Ser Leu Gln Lys Leu Asp Pro His Gln Lys Asp Asp Ile Asn Lys
465 470 475 480

Lys Ala Phe Asp Lys Phe Lys Lys Glu His Gly Val Val Pro Gln Ala
485 490 495

Asp Asn Ala Thr Pro Ser Glu Arg Phe Glu Gly Pro Tyr Thr Asp Phe
500 505 510

Thr Pro Trp Thr Thr Glu Glu Gln Lys Leu Leu Glu Gln Ala Leu Lys
515 520 525

Thr Tyr Pro Val Asn Thr Pro Glu Arg Trp Glu Lys Ile Ala Glu Ala
530 535 540

Val Pro Gly Arg Thr Lys Lys Asp Cys Met Lys Arg Tyr Lys Glu Leu
545 550 555 560

Val Glu Met Val Lys Ala Lys Lys Ala Ala Gln Glu Gln Val Leu Asn
565 570 575

Ala Ser Arg Ala Lys Lys
580